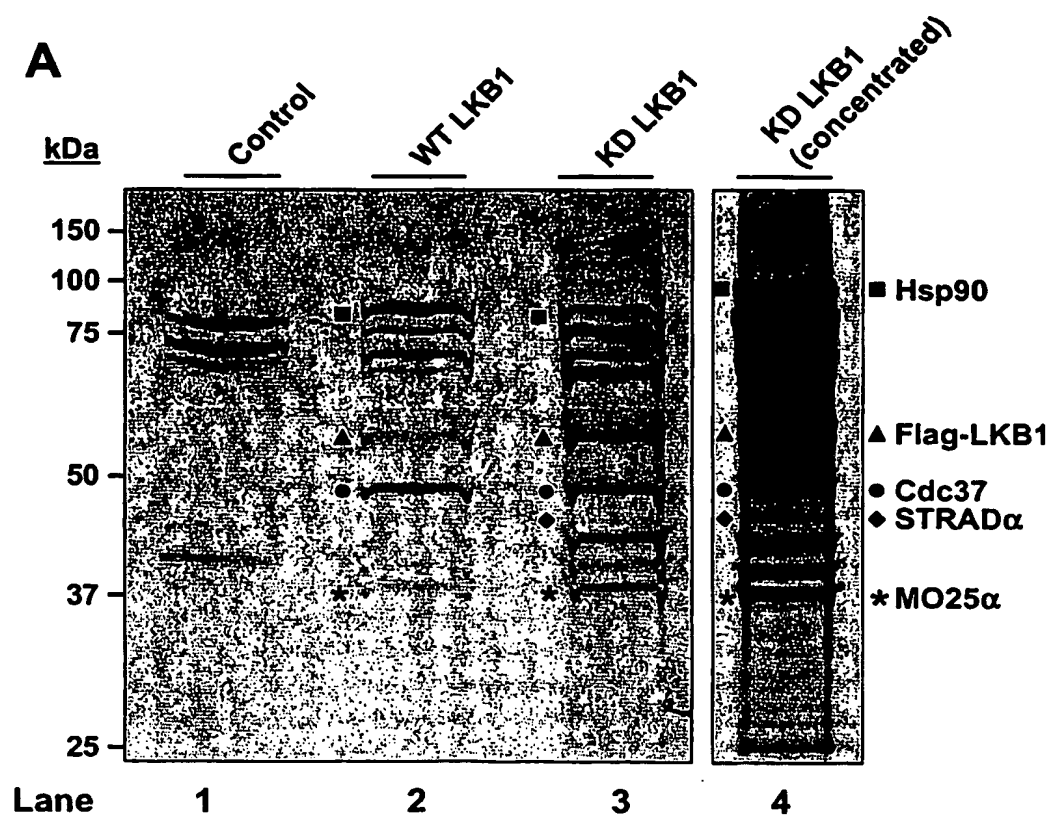


Figure 1



BEST AVAILABLE COPY

**Figure 1a****B**

|   | Protein name   | Peptide matches | % sequence coverage | NCBI gi number |
|---|----------------|-----------------|---------------------|----------------|
| ■ | Hsp90          | 15/44           | 30%                 | 20149594       |
| ▲ | Flag-LKB1      | 14/46           | 35%                 | 7106425        |
| ● | Cdc37          | 31/72           | 59%                 | 5901922        |
| ◆ | STRAD $\alpha$ | 11/80           | 34%                 | 12060855       |
| * | MO25 $\alpha$  | 17/37           | 47%                 | 7706481        |

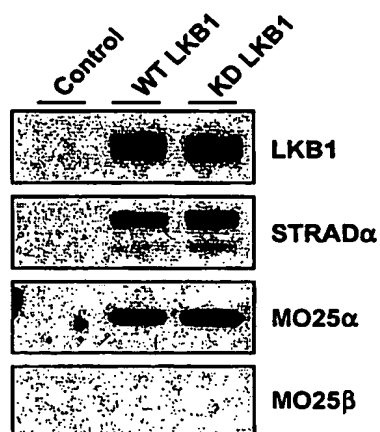
**C**

Figure 2

A

```

hMO25α  1  MPP--FSGSHKSPADIVVNCRESFAVIEROD-----ISDKPAEKATEEVSKNIWA
hMO25β  1  MPI--FSKSHKNDPAETVETIKINIAELERQ-----DKKTEKASEEVSKSLQA
dMO25   1  MPI--FGKSCKSPVFIIVKSLKPAINAHAG-----DENVEKAOHIVSKNIWS
cMO25α  1  MLKPLFGCHDHPADIVVNCRESFAVIEROD-----TNTSEKAVEKAIIEETKMAAL
cMO25β  1  MPI--LFGKSHKSPADIVVNCRESFAVIERODLPPPKLDKDGNIQSDKKHYKALIEVSKNIWA

hMO25α  50  MKETLYGI--NEKKEP-QTEAVAQIAQELYNISGLSTIADPOLIDFEGKKDVAOIFNNNI
hMO25β  46  MKETLYGI--NEKKEP-PTTEAVAQIAQELYNISGLSTIADPOLIDFEGKKDVAOIFNNNI
dMO25   46  MKETLYGI--SEAEHPADYVVAQIAQELYNISGLSTIADPOLIDFEGKKDVAOIFNNNI
cMO25α  53  ARTFEYCGDANIEPNN---EQTOLAQEYVNIIVLPALIKHHEPEFECKKDVASEFNNNI
cMO25β  60  LKSFYCGNDSAPPSSEHVVOVAQIAQELYNISGLSTIADPOLIDFEGKKDVAOIFNNNI

hMO25α  107  RRQIGTRSPTEVEYICTOQNILEMMLKGYE--SPETALNCGIMLRECIHHEPLAKIILISE
hMO25β  103  RRQIGTRSPTEVEYISATPHILEMMLKGYE--APQIAIRCCGIMLRECIHHEPLAKIILISE
dMO25   104  RRQIGTRSPTEVEYCTPEILEFTLHAGYDAHPHAIANSCTMLREGANYBALAKIIEHSE
cMO25α  110  RRQIGTRSPTEVEYDAPPEIHITLLEGYE--QPHIATCGIMLRECIHHEPLAKIILISE
cMO25β  120  RRQIGTRSPTEVEYDAPPEIHITLLEGYE--VPHIATCGIMLRECIHHEPLAKIILISE

hMO25α  165  QPRDFPEYVEHSTFDIASDAFTFKDLLTRHKHSAEFLNCHYDPEF--SEVDEKLHSENY
hMO25β  161  QPRDFPEYVEHSTFDIASDAFTFKDLLTRHKHSAEFLNCHYDPEF--EDVDEKLHSENY
dMO25   164  EPEKFFLYVEHSTFDIASDAFTFKDLLTRHKHSAEFLDANYDPEF--SOHNYDEKLHSENY
cMO25α  168  YFORFHVEVSDVFDIADAFSTFKDLMTKHKNSAEFLDNYDPEF--GQVSAITNSENY
cMO25β  178  VETTFELVQSEVFDIADAFSTFKDLMTKHKNSAEFLNCHYDPEF--AQVONLHSENY

hMO25α  224  VTRRQSLKLLGELLDRHNFETMTKYISKPENLKLMMNLLRDKSRNIQFEAFHVFKVFVA
hMO25β  220  VTRRQSLKLLGELLDRHNFETMTKYISKPENLKLMMNLLRDKSRNIQFEAFHVFKVFVA
dMO25   224  VTRRQSLKLLGELLDRHNFETMTKYISKPENLKLMMNLLRDKSRNIQFEAFHVFKVFVA
cMO25α  227  VTRRQSLKLLGELLDRHNFETMTKYISKPENLKLMMNLLRDKSRNIQFEAFHVFKVFVA
cMO25β  237  VTRRQSLKLLGELLDRHNFETMTKYISKPENLKLMMNLLRDKSRNIQFEAFHVFKVFVA

hMO25α  284  NPNKTPPIIDILLNCAKLEFLSKFQNDRTDEQFNDEKAYLIKQIQELPLPAQQA--
hMO25β  280  SPNKTQPIIDILLNCAKLEFLSKFQNDRTDEQFNDEKAYLIKQIQELPLPAQQA--
dMO25   284  NPNKTPPIIDILLNCAKLEFLSKFQNDRTDEQFNDEKAYLIKQIQELPLPAQQA--
cMO25α  287  NPNKTPPIIDILLNCAKLEFLSKFQNDRTDEQFNDEKAYLIKQIQELPLPAQQA--
cMO25β  297  NPNKTPPIIDILLNCAKLEFLSKFQNDRTDEQFNDEKAYLIKQIQELPLPAQQA--

hMO25α  -----
hMO25β  -----
dMO25   -----
cMO25α  -----
cMO25β  357  KSKEDENQEPAGPSEGPSTSQ

```

Figure 2a

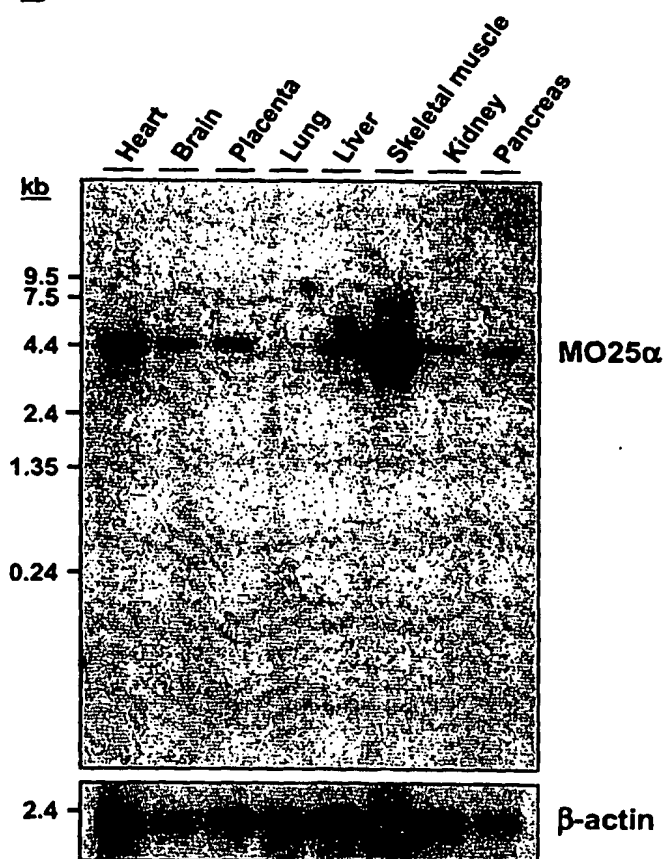
**B**

Figure 2b

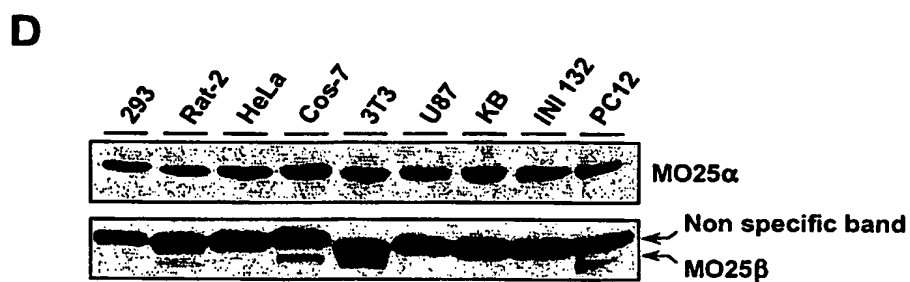
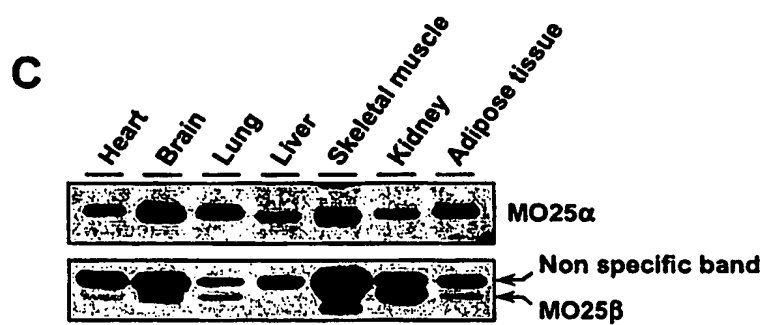


Figure 3

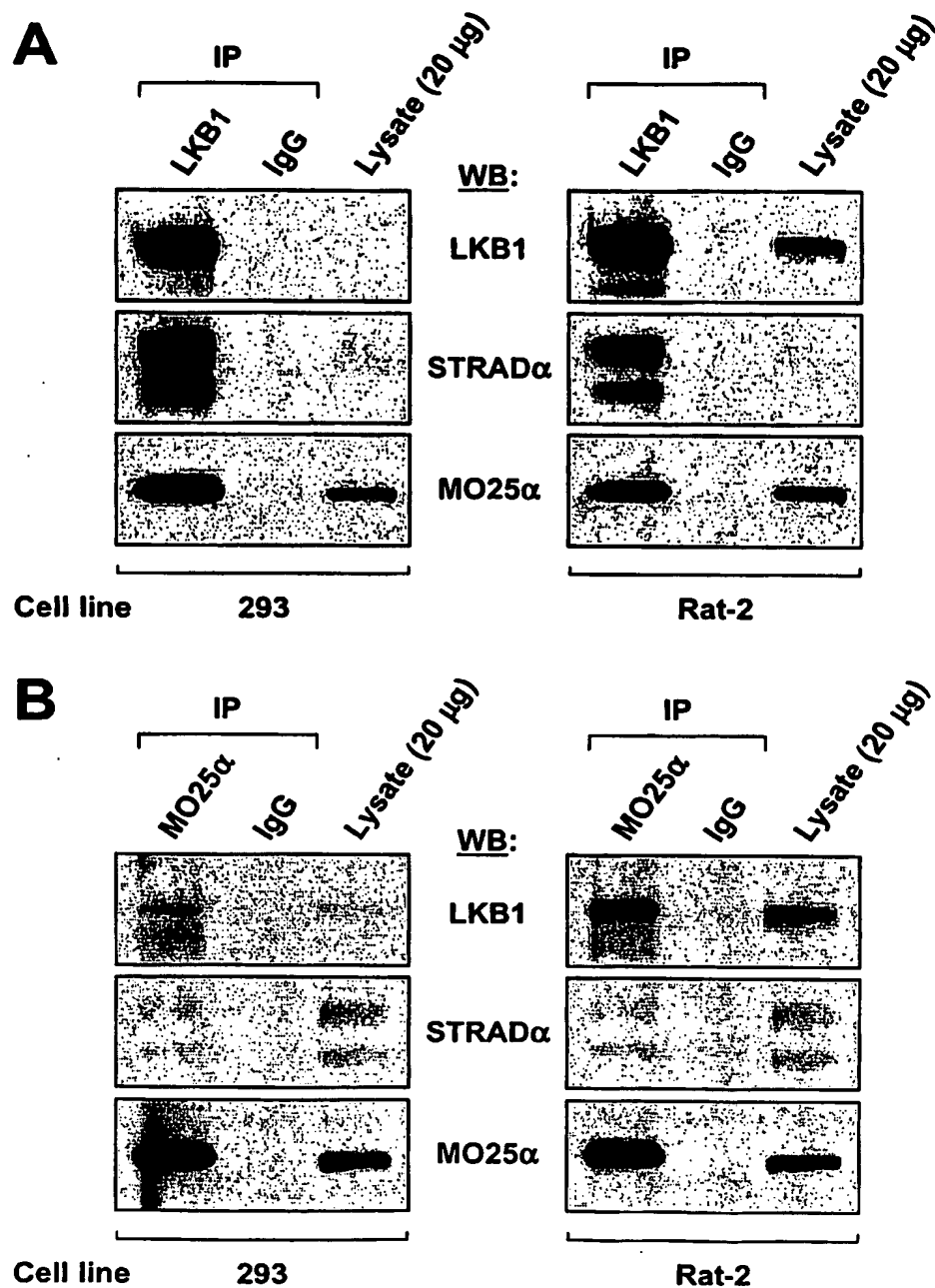


Figure 4

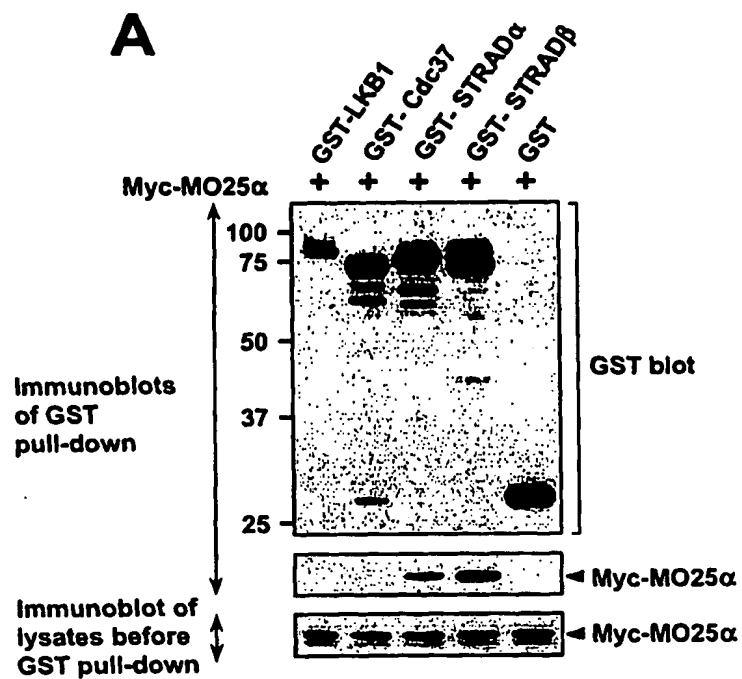
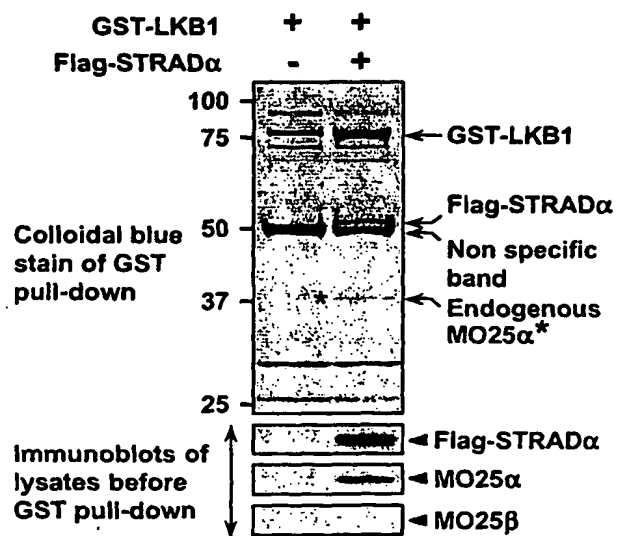
**B**

Figure 4a

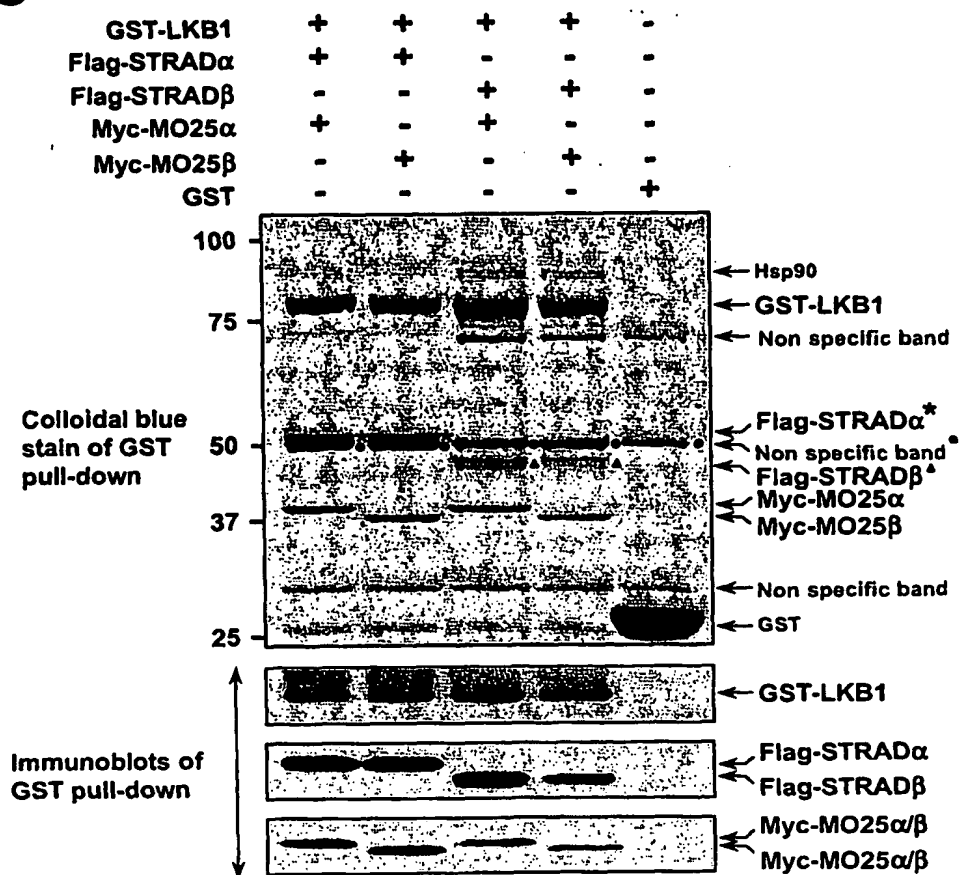
**C**



Figure 5



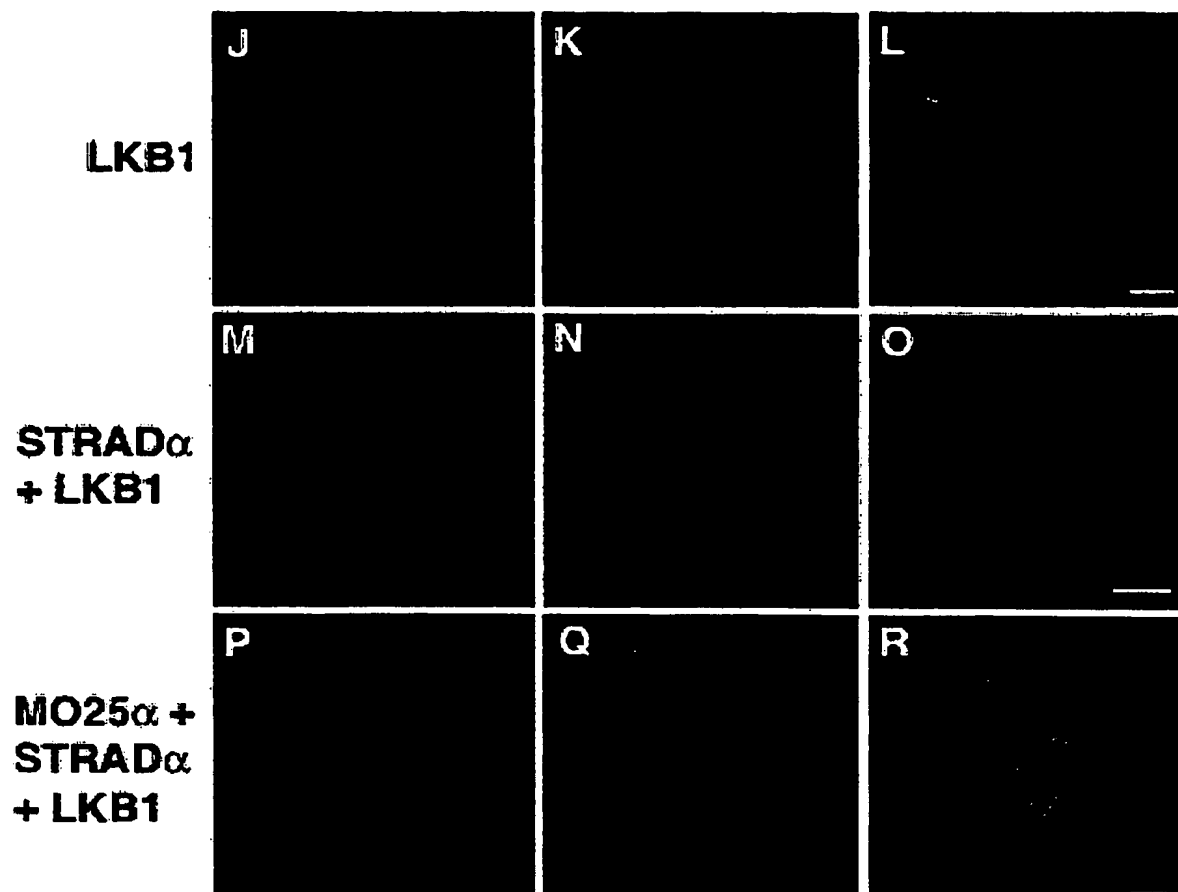
**Figure 5a**

Figure 6

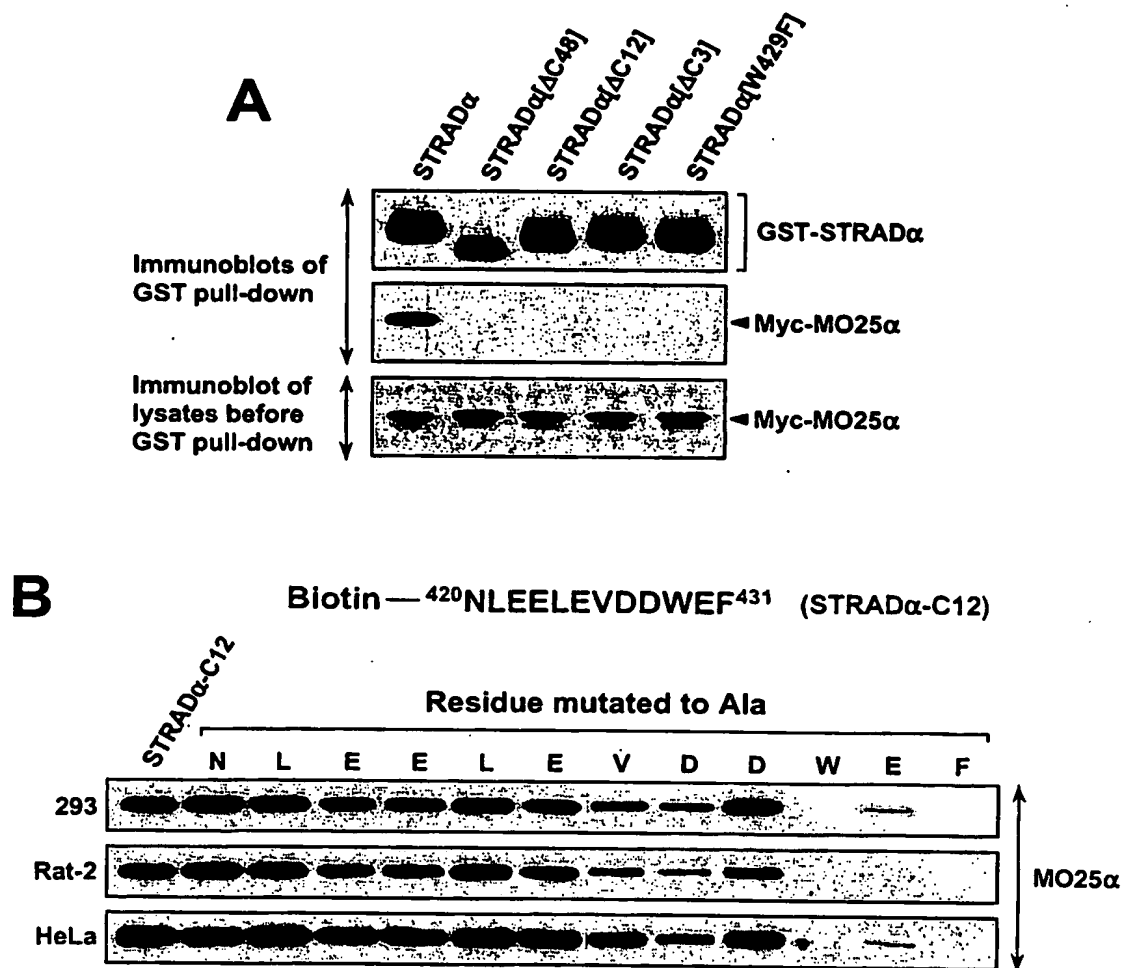


Figure 6a

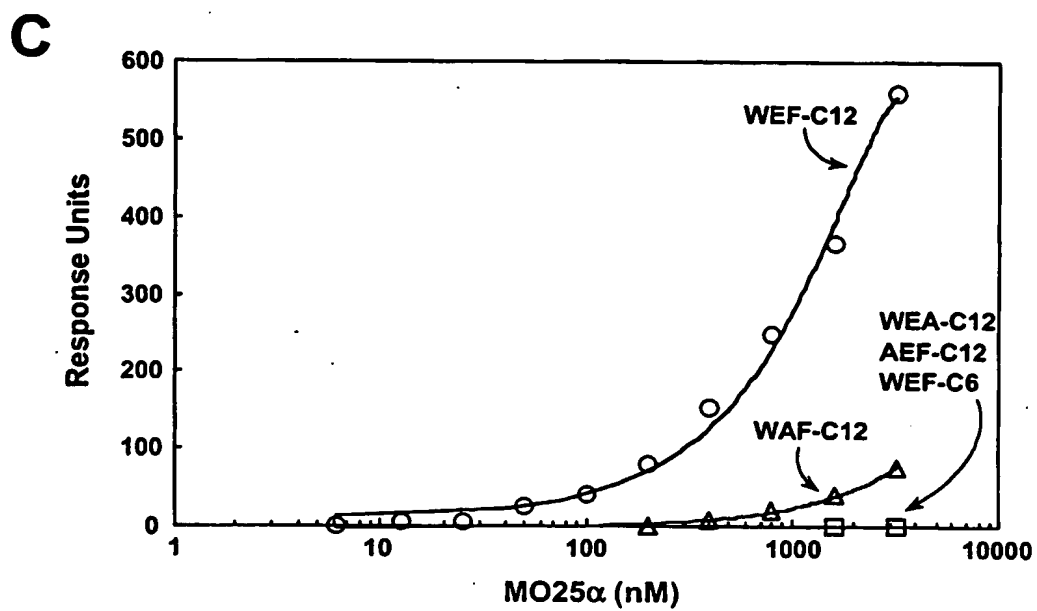




Figure 8

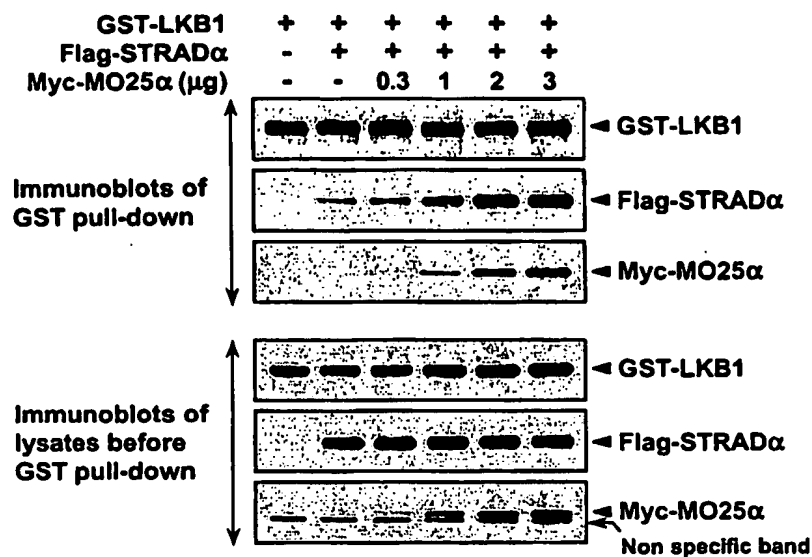
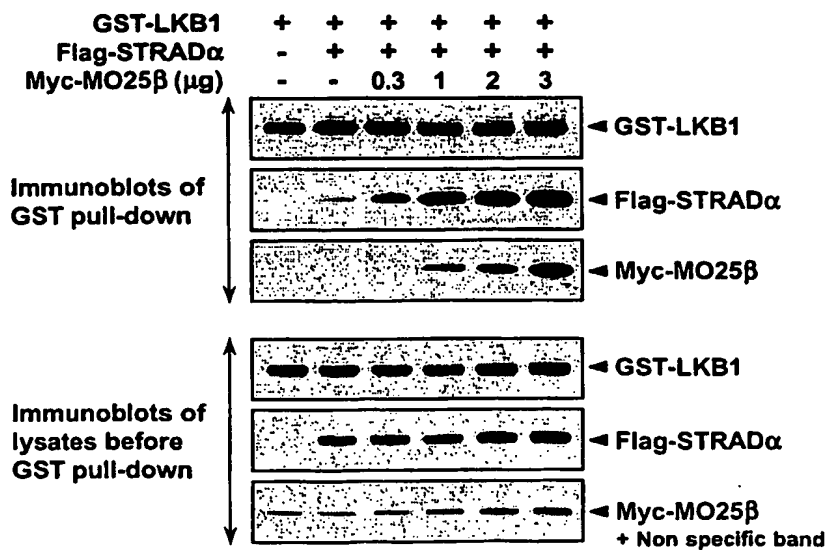
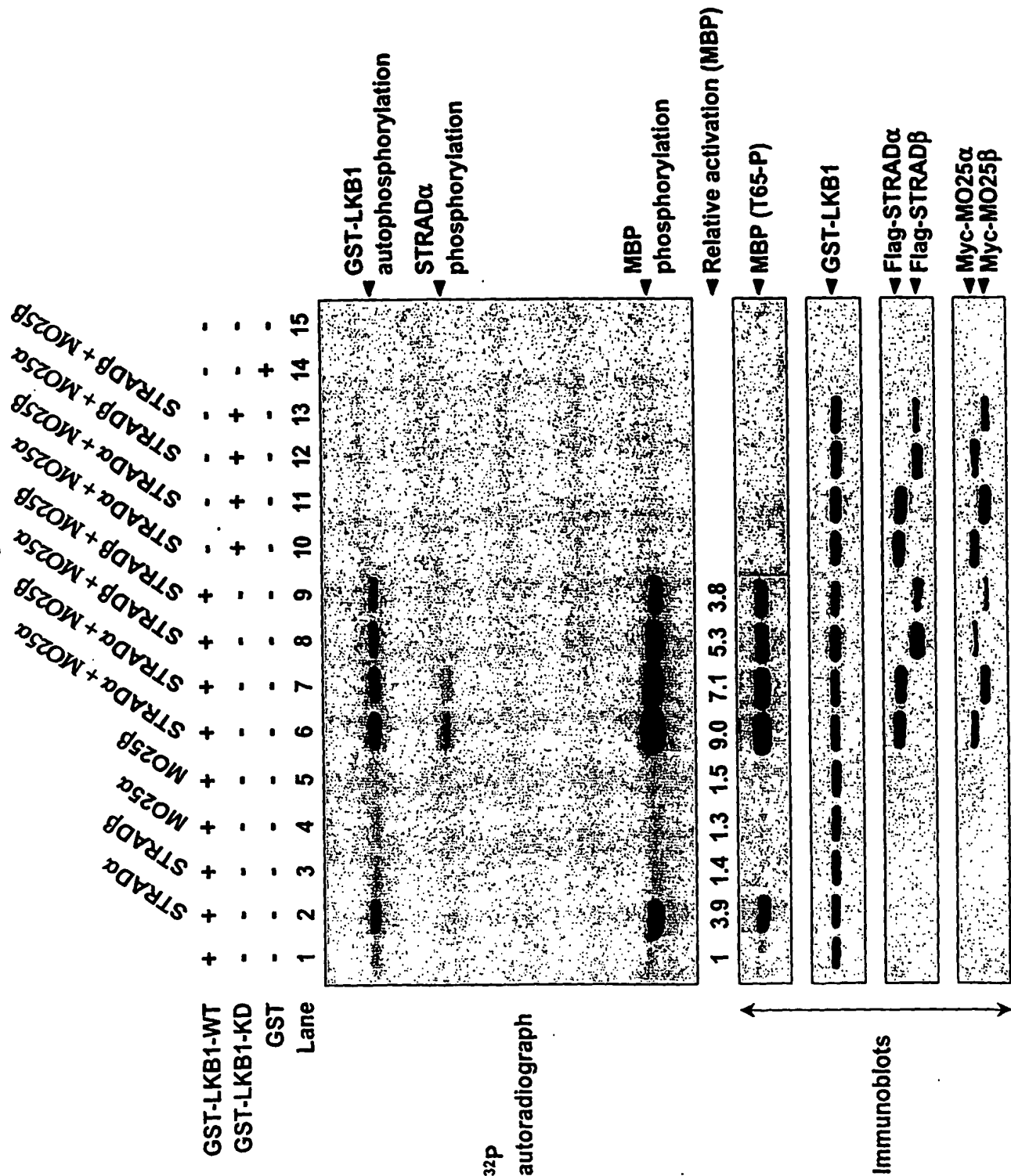
**A****B**

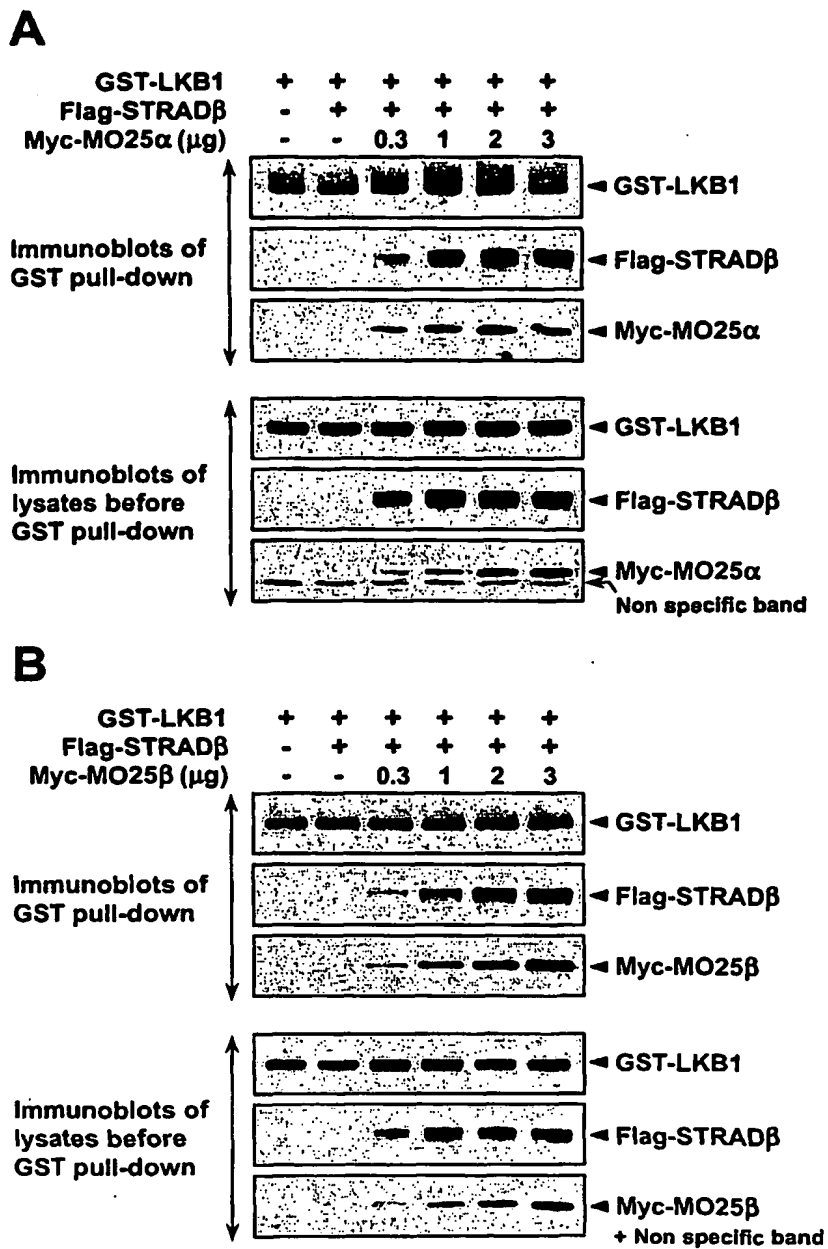
Figure 9



**SUBSTITUTE SHEET (RULE 26)**



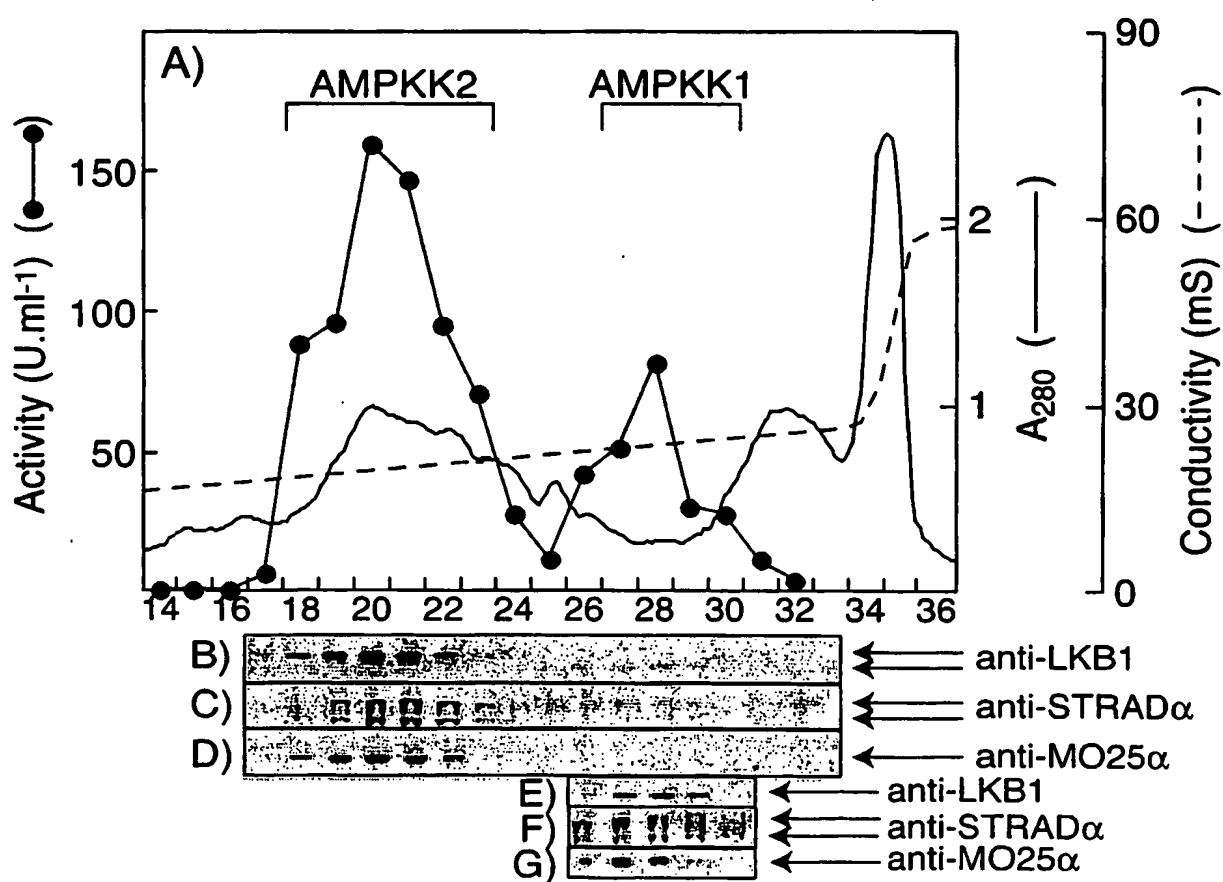
Figure 11

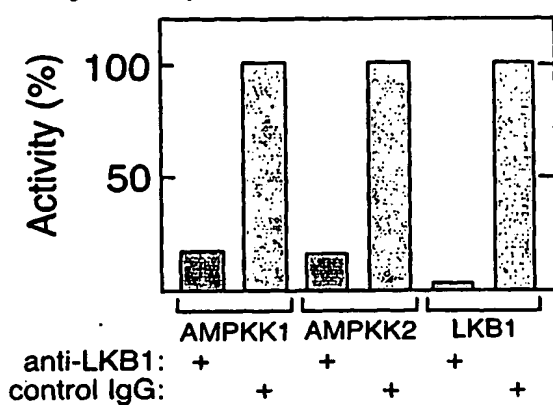
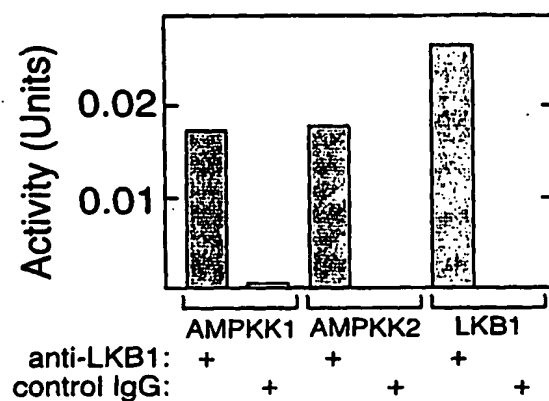
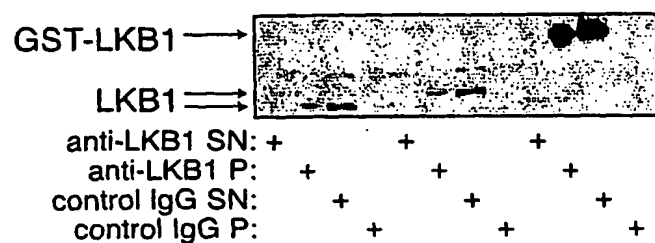
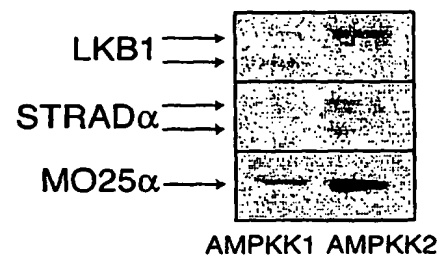


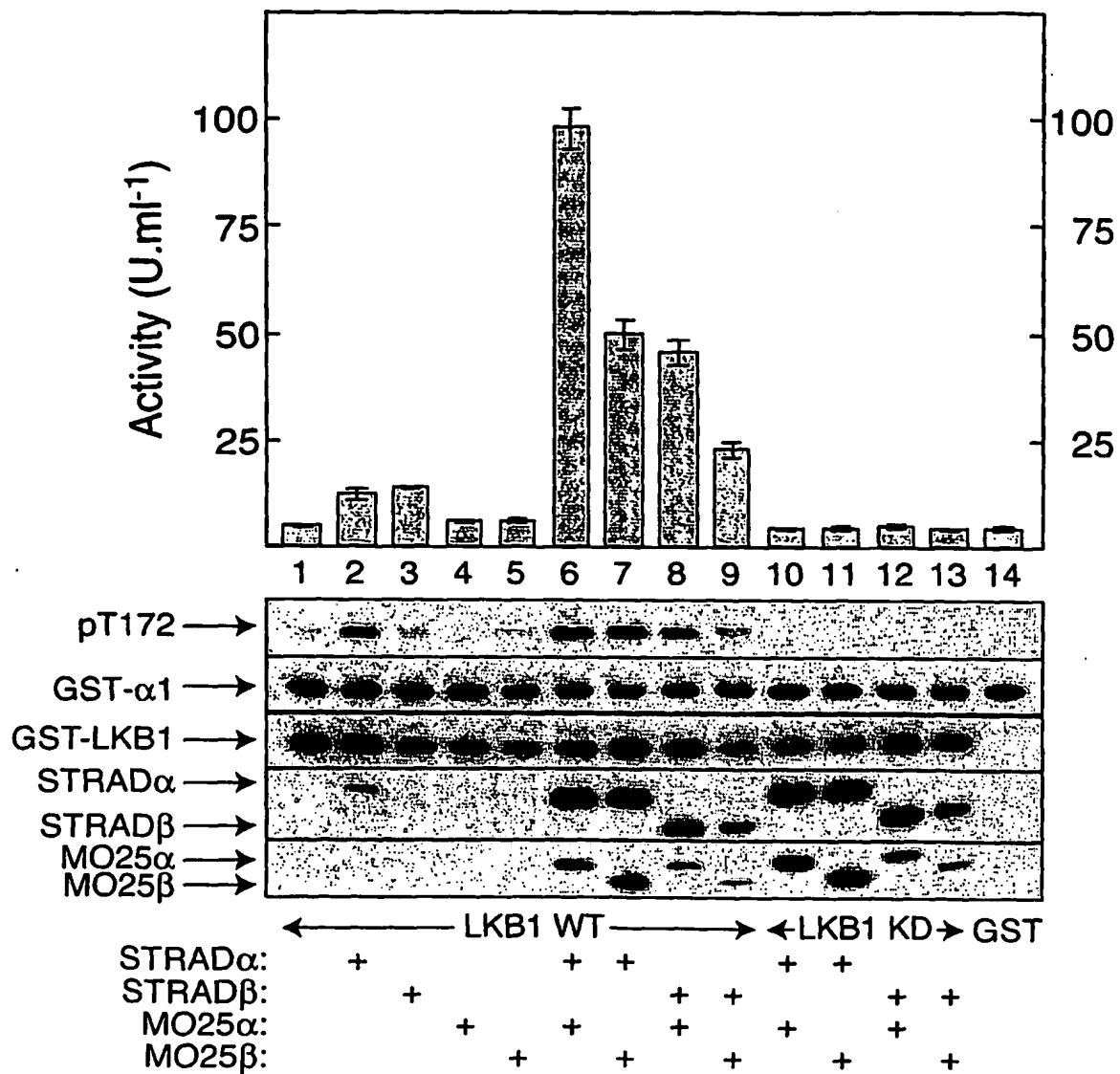
## Figure 12

|               |     |  |
|---------------|-----|--|
| Tos3          | 11  | ..LPRSSLLYNNASNSSSRIKETRKVKLLYNPLTKR.....Q...ILNNFEILATLGNGQ   |
| Pak1          | 94  | ..TPTTSSFCSSGSSKNKVKETNRISLTYPVSKR.....K...VLNTYEIIEKELGHGQ    |
| CaMKK $\beta$ | 121 | CICPSLPYSPVSSPQSSPRLPRRPTVESHHVSITGM.....QDCVQLNQYTLKDEIGKGS   |
| LKB1          | 7   | QQLGMFTEGELMSVGMDFIHRIDSTEVIYQP..RR.....KRAKLIGKYLMDLLGEGS     |
| Elm1          | 39  | TSSFGSSFSQOKPTYSTIIGENIHTILDEIRPYVKKITVSDQDKKTINQYTLGVSAGSGQ   |
| consensus     | 121 | p s s s s s rik t v l y pltkr q ilnny i lG Gq                  |
|               |     |  |
| Tos3          | 61  | YGKVKLARDLGTGALVAIKILNRFKRS....GYSL.....QLKV.EN.....           |
| Pak1          | 144 | HGKVKLARDILSKQLVAIKIVDRHEKKQRKFFTFIK.....SSKISEN.....          |
| CaMKK $\beta$ | 176 | YGVVKLAYNENDNTYYAMKVLK..KKLIRQAGFPR.....RPPRGRTRPAPGGCIQP      |
| LKB1          | 60  | YGKVKEVLDSETLCRRRAVKILK..KKLRR.....I                           |
| Elm1          | 99  | FGYVRKAYSSTLGKVAVKIIIPKKPWNAQQYSVNQVMRQIQLWKSCKGKITTNMSGNEAMR  |
| consensus     | 181 | yGkVkla d t lvAiKil k k k y k                                  |
|               |     |  |
| Tos3          | 99  | ...PRVNQEIEVMKRCHHE.NVVELYEILNDPESTKVYLVLVEYCSRGFPVKWCPENKMEI  |
| Pak1          | 187 | ...DKIKREIAIMKKCHHK.HVVQLIEVLDDLKSRKIYLVLEYCSRGVWKCPDPCMES     |
| CaMKK $\beta$ | 227 | RGPIEQVYQEIAILKKLDHP.NVVKLVEVLDDPNEDHLYMVFEVLNQGFPV.....MEV    |
| LKB1          | 89  | PNGEANVKKEIQLLRRLRHK.NVIQLVDVLYNEEKQKMYMVMEYC.....VCGMQEM.L    |
| Elm1          | 159 | LMNIEKCRWEIFAASRLRNHVHVRLEICLDSPFSESIWIVTNWCSLGELQWKRRDDDEDI   |
| consensus     | 241 | drv k EI vmkrlhh nvv lievLddp s kvylVleycs g v wc mei          |
|               |     |  |
| Tos3          | 154 | .KAVGPSILTFQQ....SRKVVLDVVSGLEYLHSGGITHRDIKPSNLLISSNGTV.KISD   |
| Pak1          | 242 | .DAKGPSLLSFQE....TREILRGVVLGLEYLHYQGIIHRDIKPANLLISGDGTV.KISD   |
| CaMKK $\beta$ | 279 | .PTLKP..LSEDQ....ARFYFQDLIKGIEYLHYQKIIHRDIKPSNLLVGEDGHI.KIAD   |
| LKB1          | 141 | .DSVPEKRFPVCQ....AHGYFCQLIDGLEYLHSGGIVHKDIKPGNLLLTGGTL.KISD    |
| Elm1          | 219 | LPQWKIVISNCSVSTFAKKILEDMTKGLEYLHSGGCIHRDIKPSNILLDEEEKVAKLSD    |
| consensus     | 301 | v p ils q ar vv dvv GLEYLHsQgiiHrDIKPSnLLis dgtv KisD          |
|               |     |  |
| Tos3          | 208 | FG..VAM.STATGSTNIQSSHEQLLKSRA LGTPAFFAPELCSTEKEY.....          |
| Pak1          | 296 | FG..VSLAASSTNSSDSSESLELAKTVGTPAFFAPEMCLGEDAFTRYNLTKENLFRG      |
| CaMKK $\beta$ | 331 | FG..V.....SNEFKGS..DALLSNTVGTAPAFMAPESLS.....ETRKIFSG          |
| LKB1          | 195 | LG..VAEALHPFAADDTCRTSQ.....GSPAFQPPEIANGLDTFE.....             |
| Elm1          | 279 | FGSCIFTQSLPFS DANFEDCFQRELNKIVGTAPAFIAPELCHLGNSKRDFVTD.....    |
| consensus     | 361 | fG v t s d s l r vGtPAF aPElc y                                |
|               |     |  |
| Tos3          | 252 | SC.SSAIDIWSLGVTIYCLLFGKLPFNANSGLLEFDSIINKPLEFFPSYEEMLNATSGIT   |
| Pak1          | 354 | SCISFMIDIWAVGVTLYCLLFGMLPFFSDFELKLFKEKIVNDPLKFPTFKEIQSNKVS KVS |
| CaMKK $\beta$ | 369 | K...ALDVWAMGVTLYCFVFGQCFPMDERIMCLHSKIKSQALEFPDQPDIA.....       |
| LKB1          | 233 | ...GFKVDIWSAGVTLYNITTGLYPFEGDNIYKLFENIGKGSYAIP.....            |
| Elm1          | 332 | ...GFKLDIWSLGVTIYCLLYNELPFFGENEFETYHKIIEVSLSSKINGNTLNDLVIKRL   |
| consensus     | 421 | f iDiWslGVTIYcllfg lPF ad l lfdkIi l fp em                     |
|               |     |  |
| Tos3          | 311 | M.EEYT...DAKDLLKKLLQKDPDKRIKLADIKVHPFMC....HYGKSDAASVL...TN    |
| Pak1          | 414 | CEEEYE...MAKDLLKLLLEKNPQKRMTIPA IKKHFPVS.WDFDHPV ENDEKLLS...SV |
| CaMKK $\beta$ | 417 | ....E...DLKDLITRMLDKNPESRIVVPEIKLHPWVTRHGAEPLPSEDENCTLVEVTE    |
| LKB1          | 276 | .GDCGP...PLS DLLKGMLEYEPAKRFSIRQIRQHSWFRK...KHPPAEAPVPIPPSPDT  |
| Elm1          | 389 | LEKDVTLRISIQDLVKVLSRDQPIDSRNHSQISSSS.VNPVRNEGVPVRRFFGRLLTKKGK  |
| consensus     | 481 | ee lkDLlkkllleknP kri l Ik hpfv dh p d vl t                    |
|               |     |  |
| Tos3          | 359 | LETFHELVSPPP.....SSCKRVELVSLPVNSSFASLDSVYMFNFDHNNLRGTGADRNS    |
| Pak1          | 467 | LE..QKLRF.....QCNQTDQFE.PISISKHELKNAV.....SGVGKKIKESV          |
| CaMKK $\beta$ | 469 | EEVENSVKHIPSLATVILVKTMIRKRSFGNPFEGSRREERSLSAPGNLLTKQGS EDNLQG  |
| LKB1          | 329 | KDRWRSMTVPYLEDLHGADEDEDLFDIEDDIIYTQDFTVPGQVP EEEASHNGQRRGLPK   |
| Elm1          | 448 | KKTSGKGKDKVLVSATSKVTF SIHIDEEDPKECFSTTVLRSSPDSSDYCSSIGEEAIQVT  |
| consensus     | 541 | e lk p l rve pv s lks s lg                                     |

Figure 13



**Figure 14****A) Activity in supernatant****C) Activity in pellet****B) Immunoprecipitation of polypeptides****D) Immunoblotting of pellets**

**Figure 15****A) Activation of AMPK $\alpha$ 1 catalytic domain by LKB1**

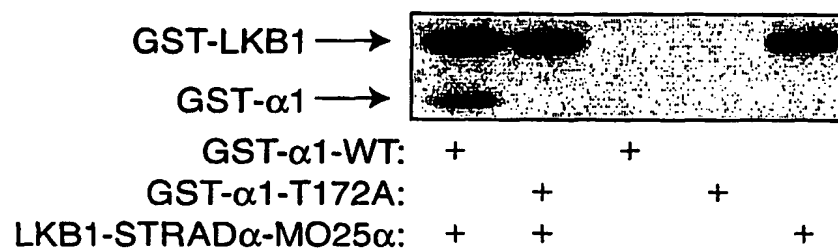
**Figure 15a****B) Phosphorylation of AMPK $\alpha$ 1 catalytic domain by LKB1**

Figure 16

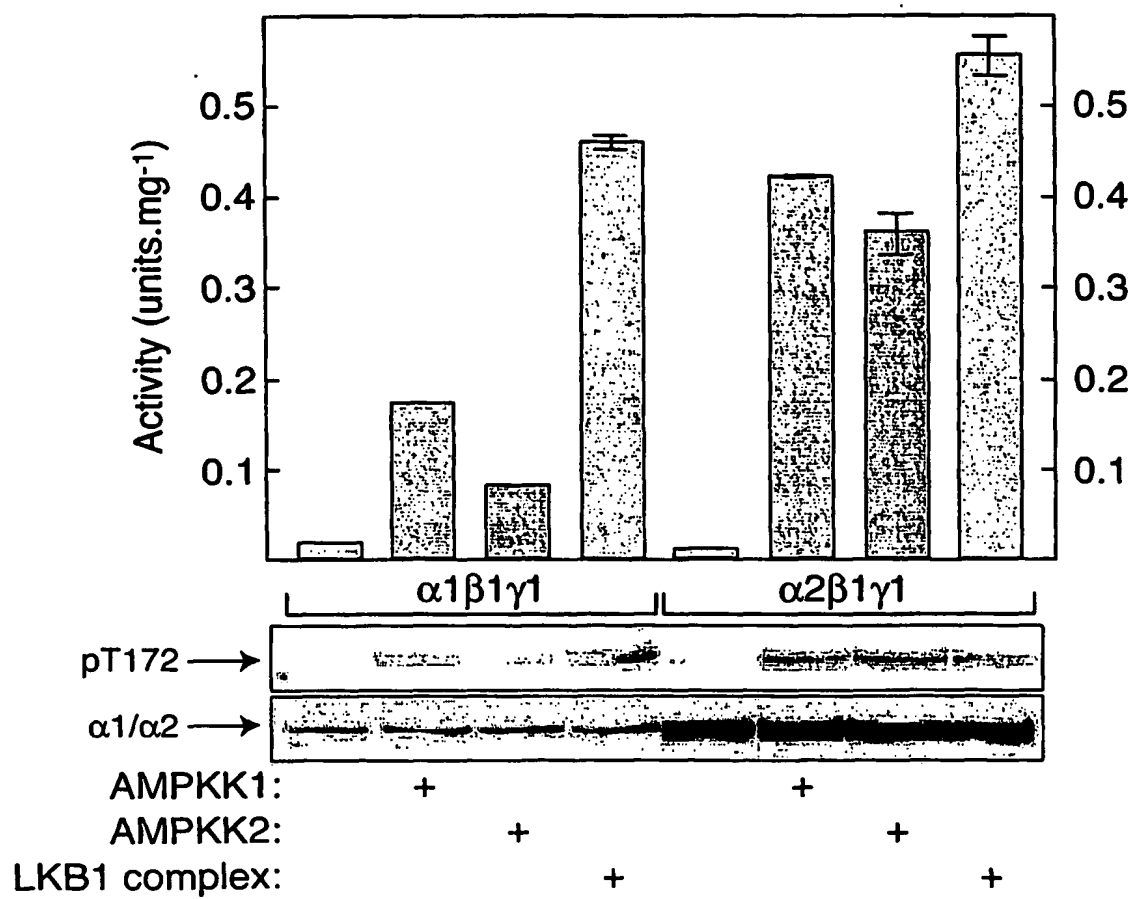


Figure 17

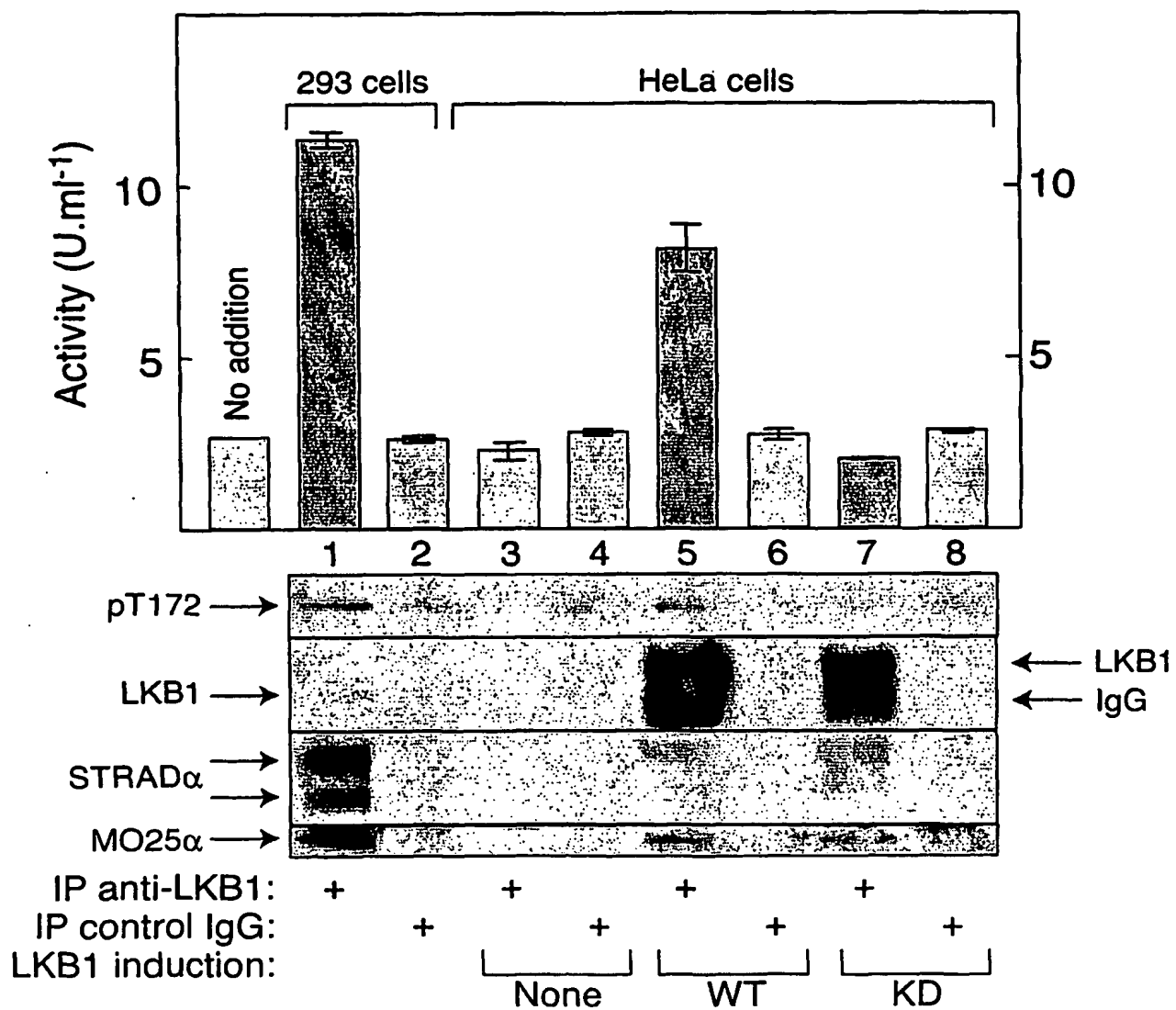




Figure 18

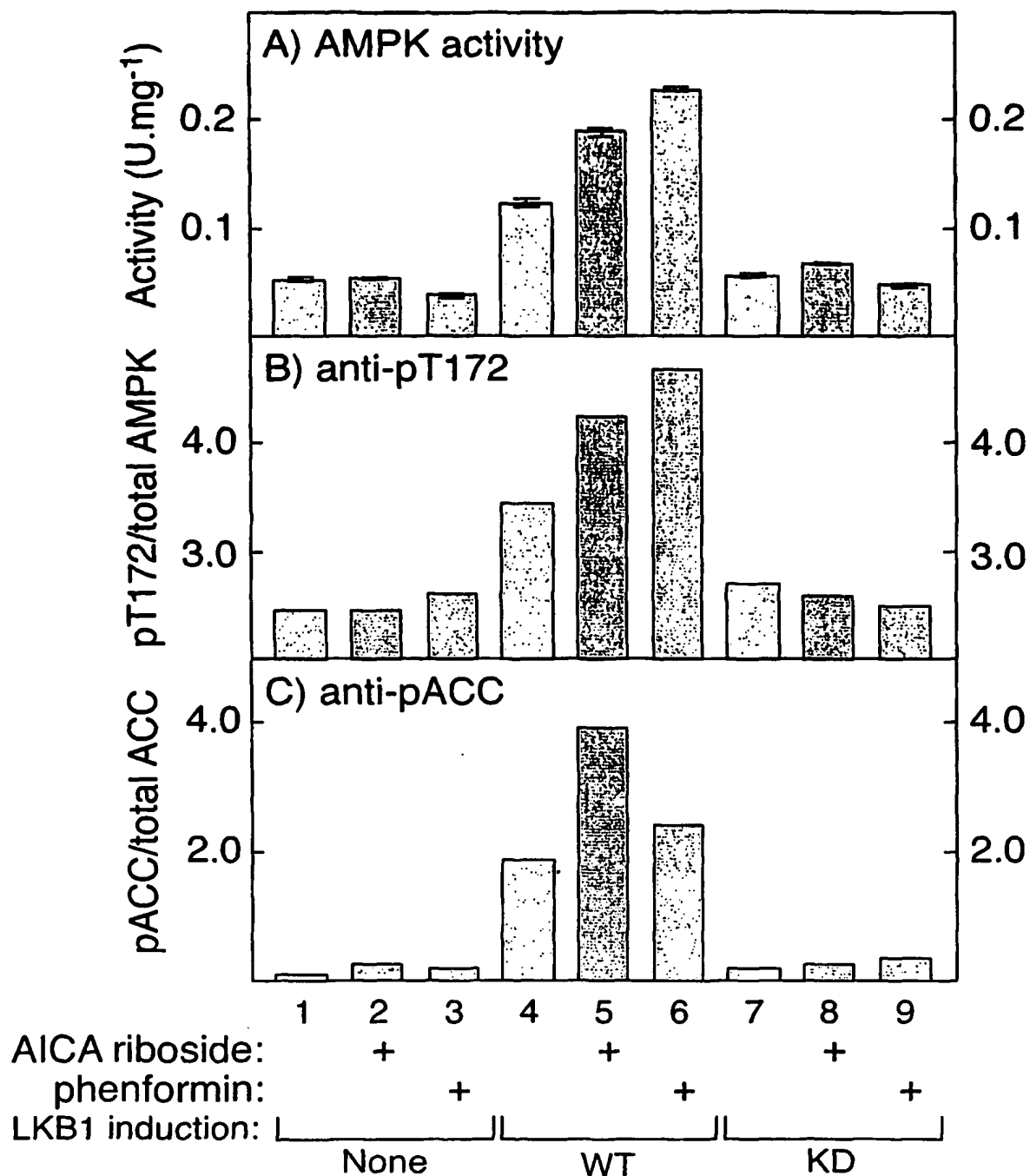
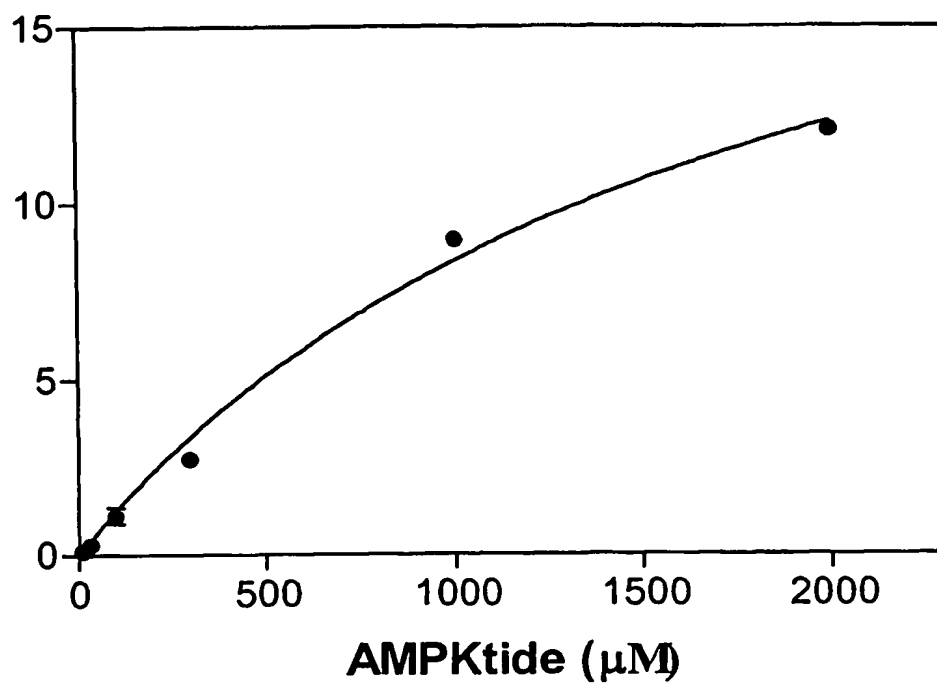


Figure 19

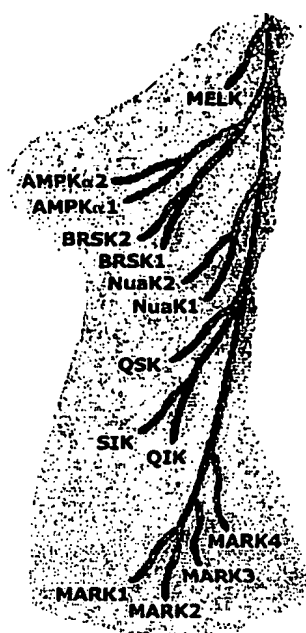
|                     |     |                   |            |     |         |      |         |    |   |   |
|---------------------|-----|-------------------|------------|-----|---------|------|---------|----|---|---|
|                     |     |                   | -11<br>-12 | -10 | -9      | -5   | -3      | -2 | P |   |
|                     |     |                   | ↓          | ↓   | ↓       | ↓    | ↓       | ↓  | ↓ |   |
| PKA-C $\alpha$      | 239 | DFGFAKR..V.KG.RTW | TL         | CGT | PEYLAPE |      |         |    |   |   |
| PKC $\alpha$        | 539 | DFGMCKEHMM.DGV    | T          | TR  | TF      | CGT  | PDYIAPE |    |   |   |
| NuaK1               | 196 | DFGLSNLYQKDK..    | FL         | QT  | FC      | GS   | PLYASPE |    |   |   |
| NuaK2               | 237 | DFGLSNLYHQGK..    | FL         | QT  | FC      | GS   | PLYASPE |    |   |   |
| BrsK1               | 190 | DFGMASLQVGDS..    | L          | L   | E       | T    | S       | C  | G | S |
| BrsK2               | 159 | DFGMASLQVGDS..    | L          | L   | E       | T    | S       | C  | G | S |
| SIK                 | 167 | DFGFGNFYKSGE..    | P          | L   | S       | T    | W       | C  | G | S |
| QIK                 | 160 | DFGFGNFFKSGE..    | L          | L   | A       | T    | W       | C  | G | S |
| AtSnRK1- $\alpha$ 1 | 160 | DFGLSNIMRDGH..    | FL         | K   | T       | S    | C       | G  | S | P |
| AtSnRK1- $\alpha$ 2 | 161 | DFGLSNVMRDGH..    | FL         | K   | T       | S    | C       | G  | S | P |
| AMPK- $\alpha$ 1    | 159 | DFGLSNMMSDGE..    | FL         | R   | T       | S    | C       | G  | S | P |
| AMPK- $\alpha$ 2    | 157 | DFGLSNMMSDGE..    | FL         | R   | T       | S    | C       | G  | S | P |
| ScSnf1              | 195 | DFGLSNIMTDGN..    | FL         | K   | T       | S    | C       | G  | S | P |
| QSK                 | 206 | DFGFSNLFTPGQ..    | L          | L   | K       | T    | W       | C  | G | S |
| MELK                | 150 | DFGLCAKPKGNKDYH   | L          | Q   | T       | C    | C       | G  | S | L |
| consensus           | 243 | DFGlsnl           | g          | fL  | Ts      | CGSp | YAaPE   |    |   |   |

**Figure 20**

**$K_m: 1.80 \pm 0.48$**

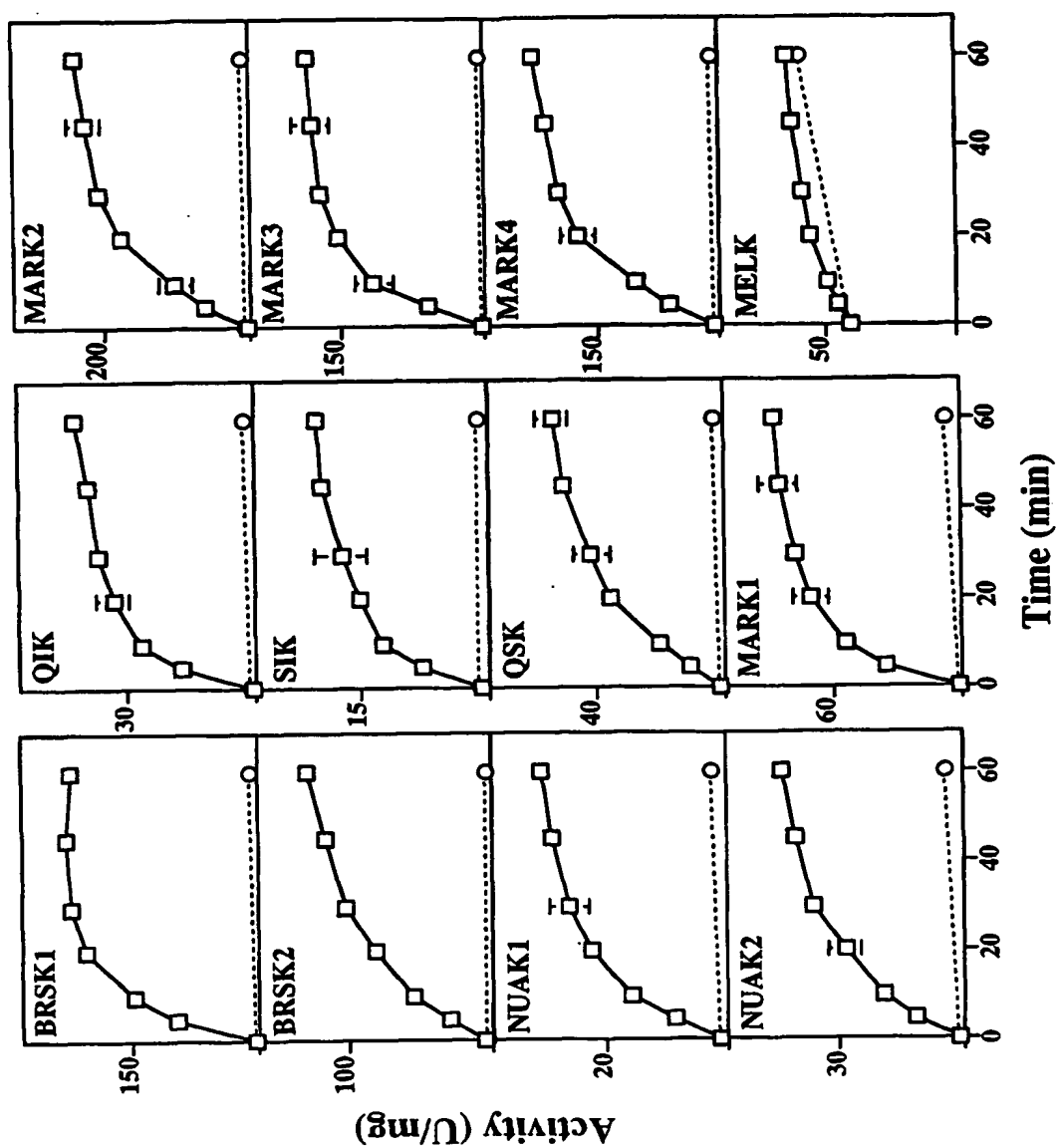
**$V_{max}: 23.43 \pm 3.51 \text{ U/mg}$**

Figure 21



|       |     |                                |   |   |
|-------|-----|--------------------------------|---|---|
| AMPK1 | 159 | DFGLSNMMSDGE--FLRTSCGSPNYAAPE  | * | * |
| AMPK2 | 157 | DFGLSNMMSDGE--FLRTSCGSPNYAAPE  |   |   |
| BRSK1 | 174 | DFGMASLOVGDS--LLETSCGSPHYACPE  |   |   |
| BRSK2 | 159 | DFGMASLOVGDS--LLETSCGSPHYACPE  |   |   |
| NUAK1 | 196 | DFGLSNLYQKDK--FLQTECGSPLYASPE  |   |   |
| NUAK2 | 193 | DFGLSNLYHQGK--FLQTECGSPLYASPE  |   |   |
| SIK   | 167 | DFGFGNIFYKSGE--PLSTWCGSPPYAAPE |   |   |
| QIK   | 160 | DFGFGNFFKSGE--LLATWCGSPPYAAPE  |   |   |
| QSK   | 206 | DFGFSNLFITPCQ--LLKTWCGSPPYAAPE |   |   |
| MARK1 | 200 | DFGFSNEFTVGN--KLDTECGSPPYAAPE  |   |   |
| MARK2 | 160 | DFGFSNEFTVGN--KLDTECGSPPYAAPE  |   |   |
| MARK3 | 196 | DFGFSNEFTVGG--KLDTECGSPPYAAPE  |   |   |
| MARK4 | 198 | DFGFSNEFTLGS--KLDTECGSPPYAAPE  |   |   |
| MELK  | 150 | DFGLCAKPKGNKDYHLQTCGSLAYAAPE   |   |   |

Figure 21A



30/38  
Figure 22

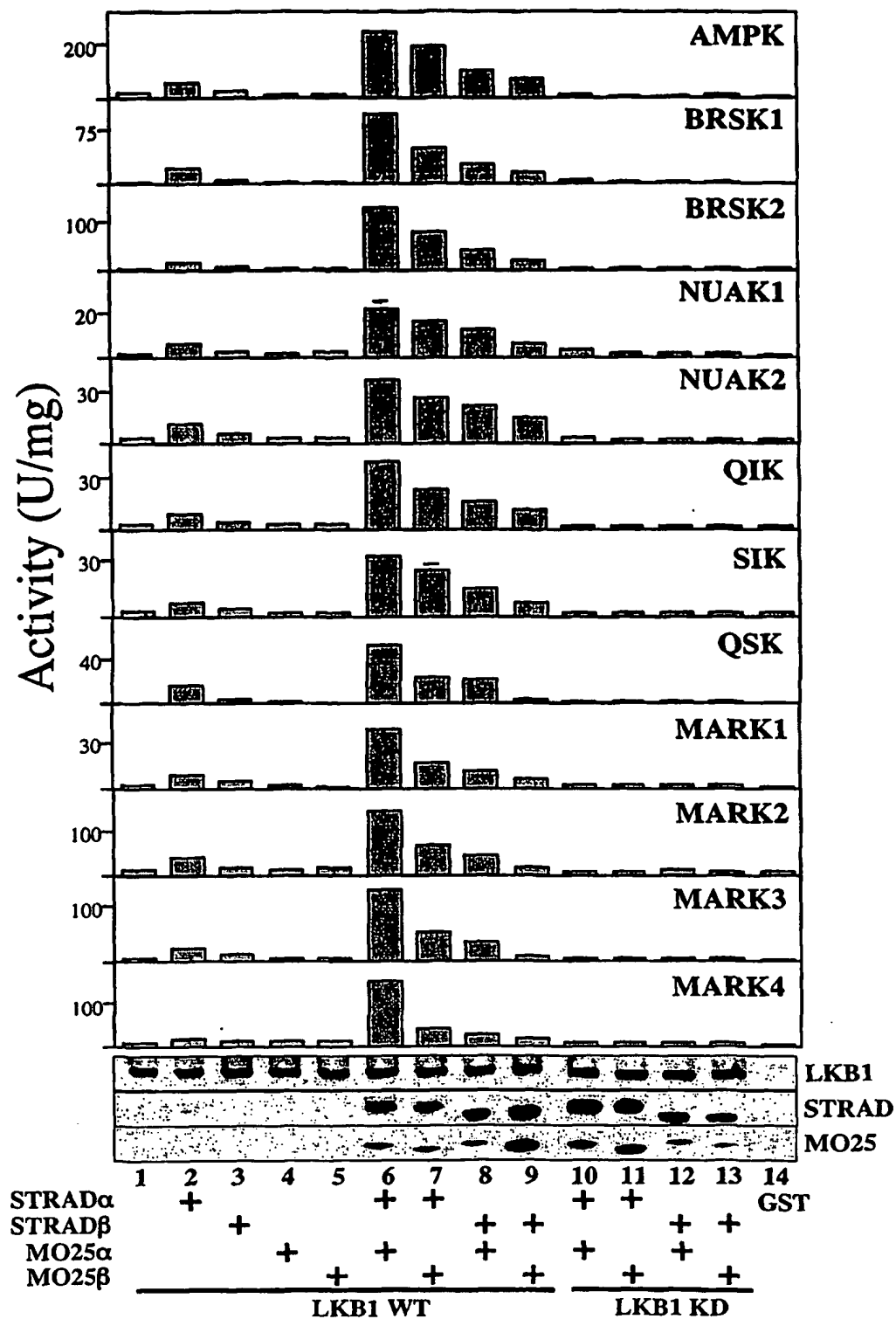


Figure 23

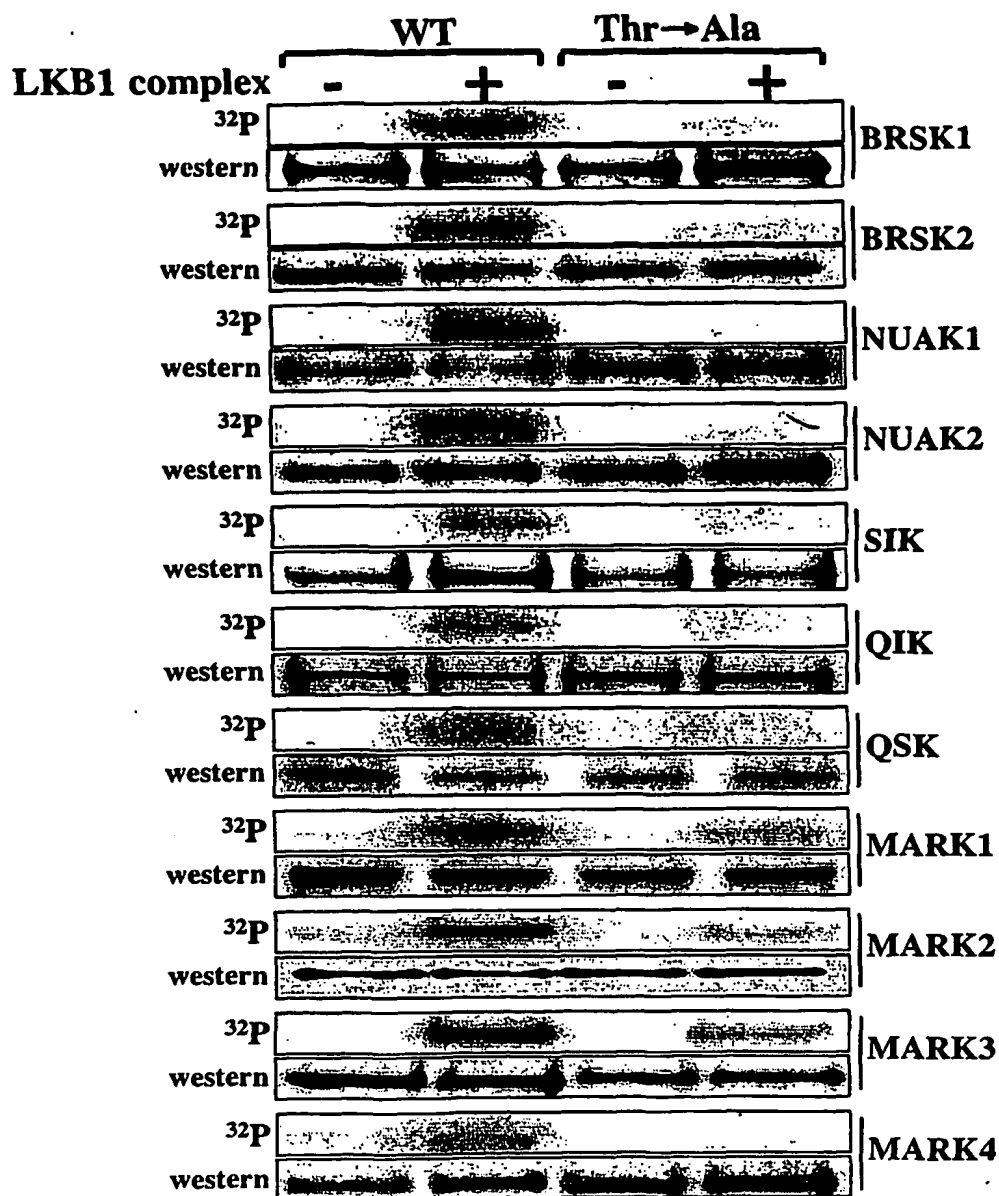


Figure 24

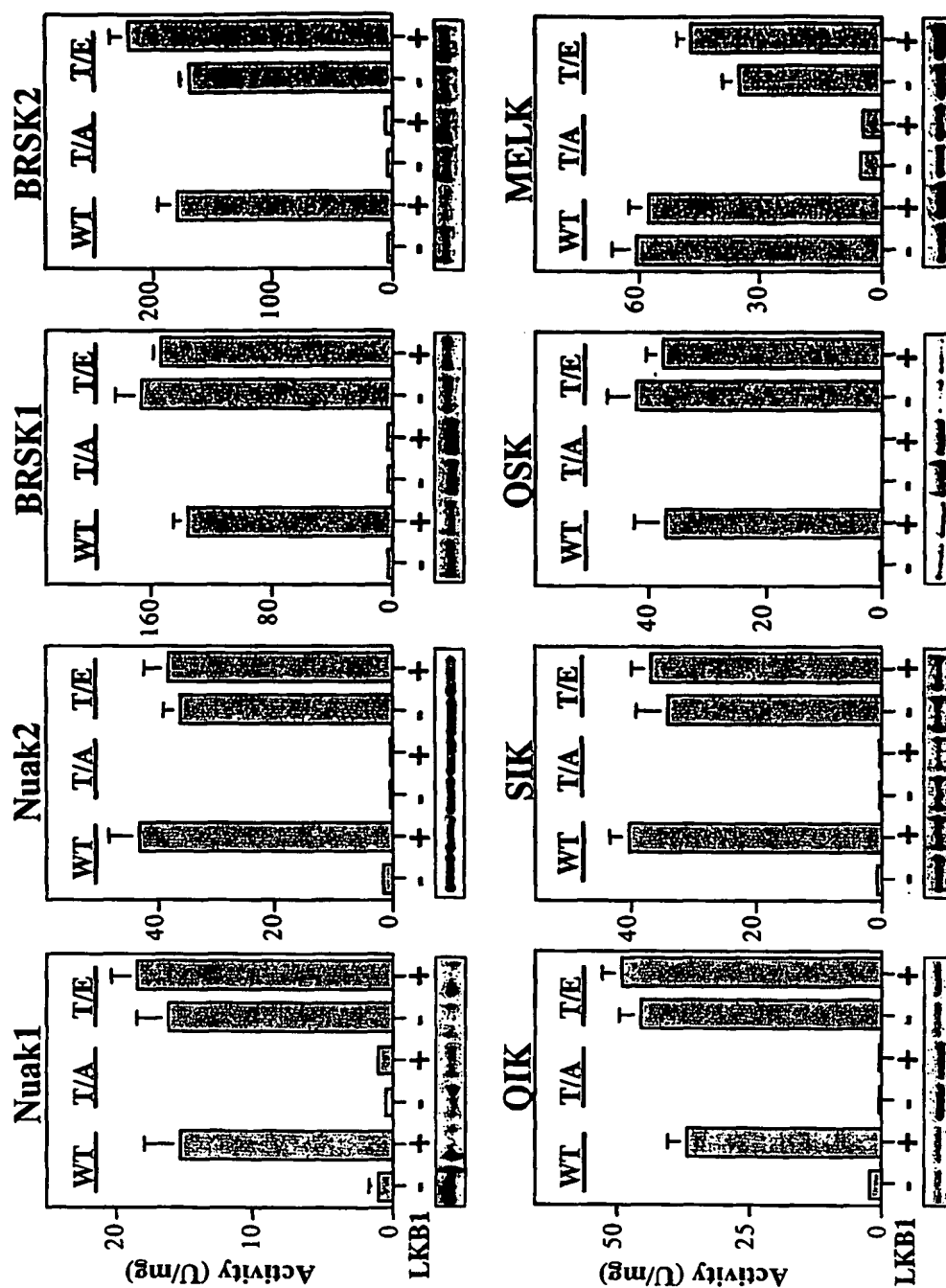




Figure 25

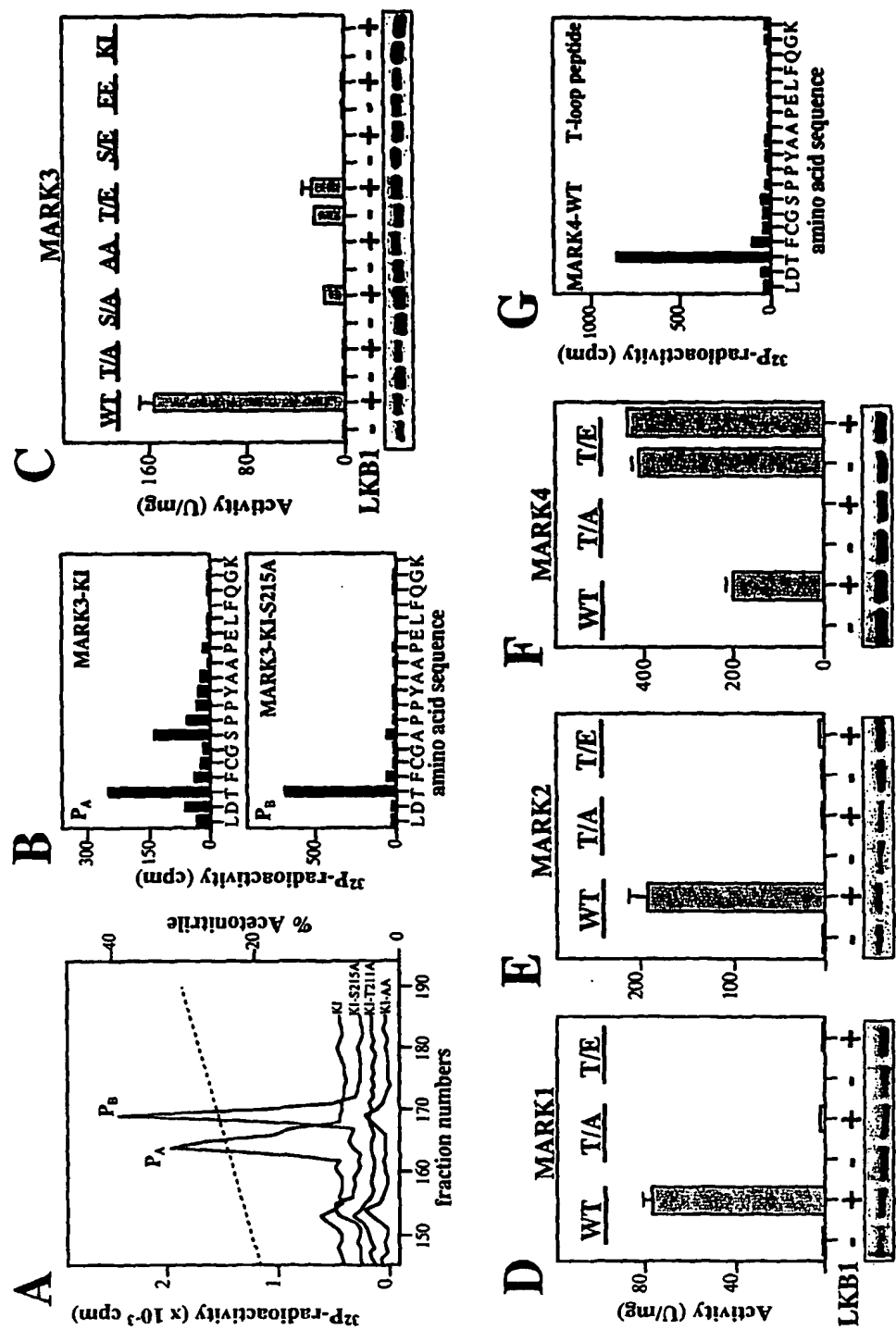


Figure 26

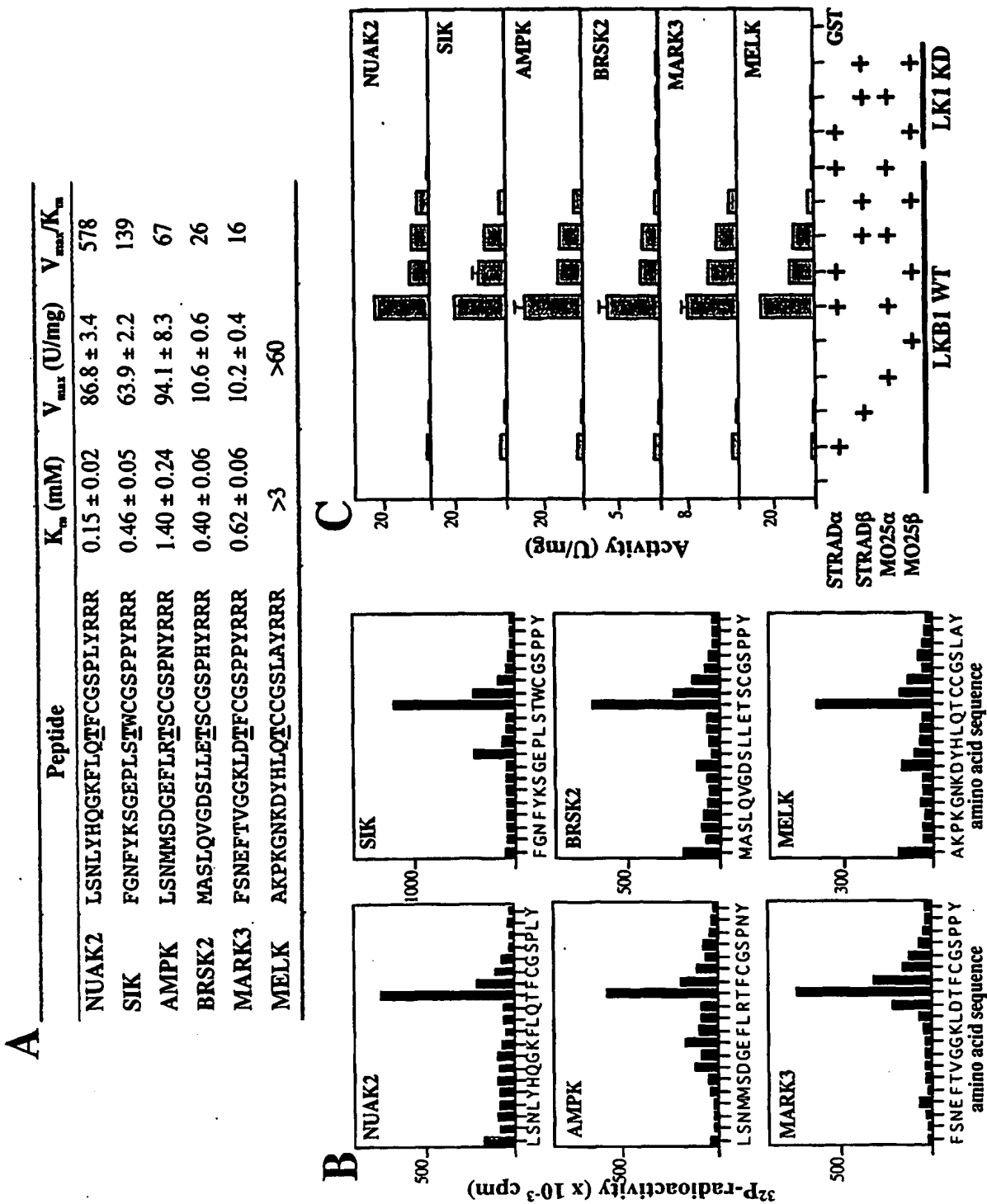


Figure 27

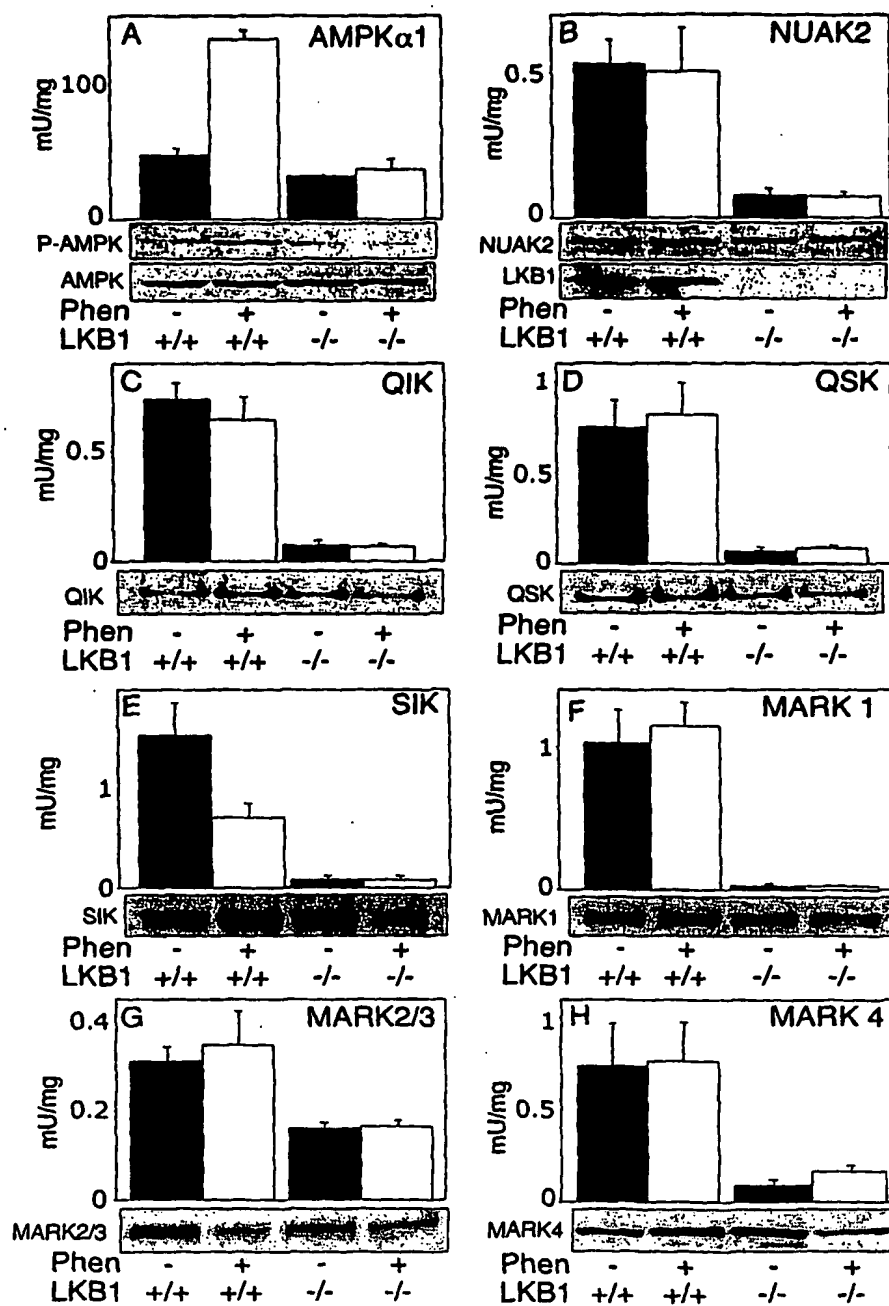


Figure 28

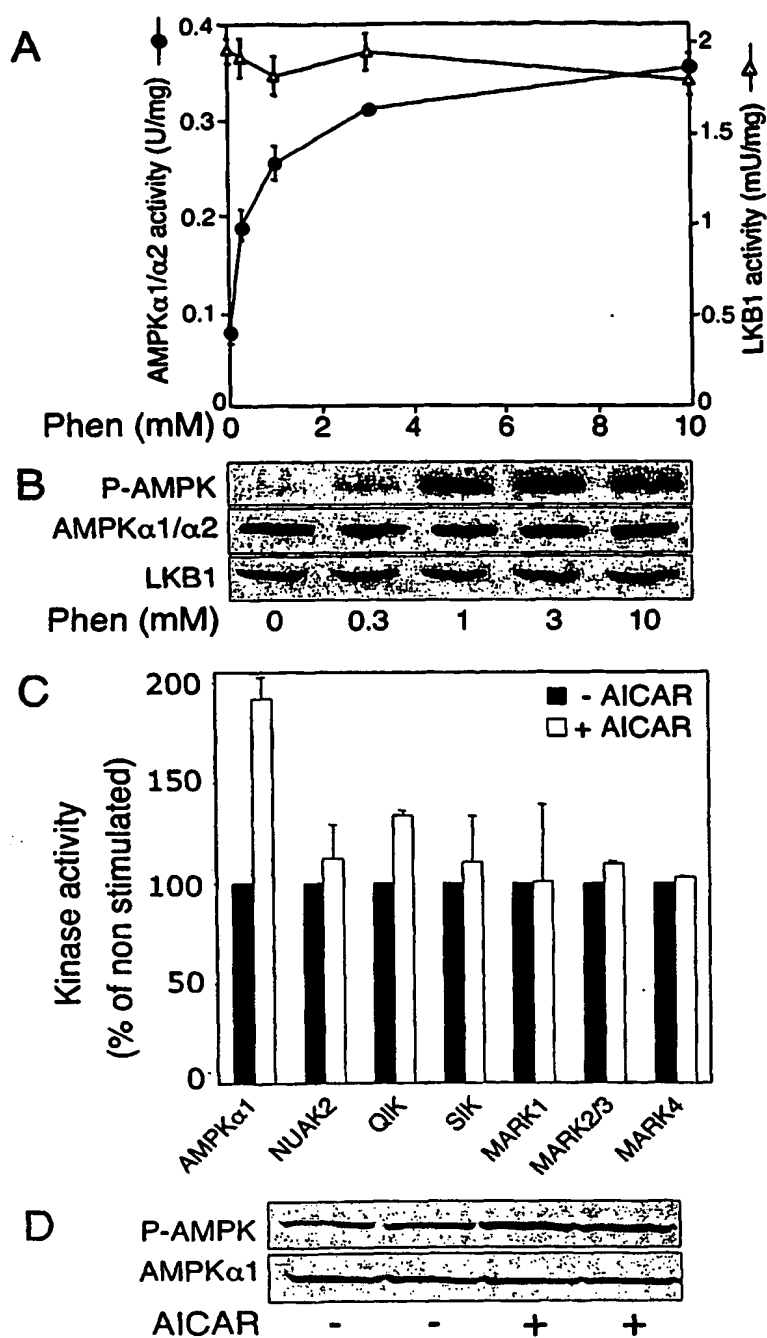


Figure 29

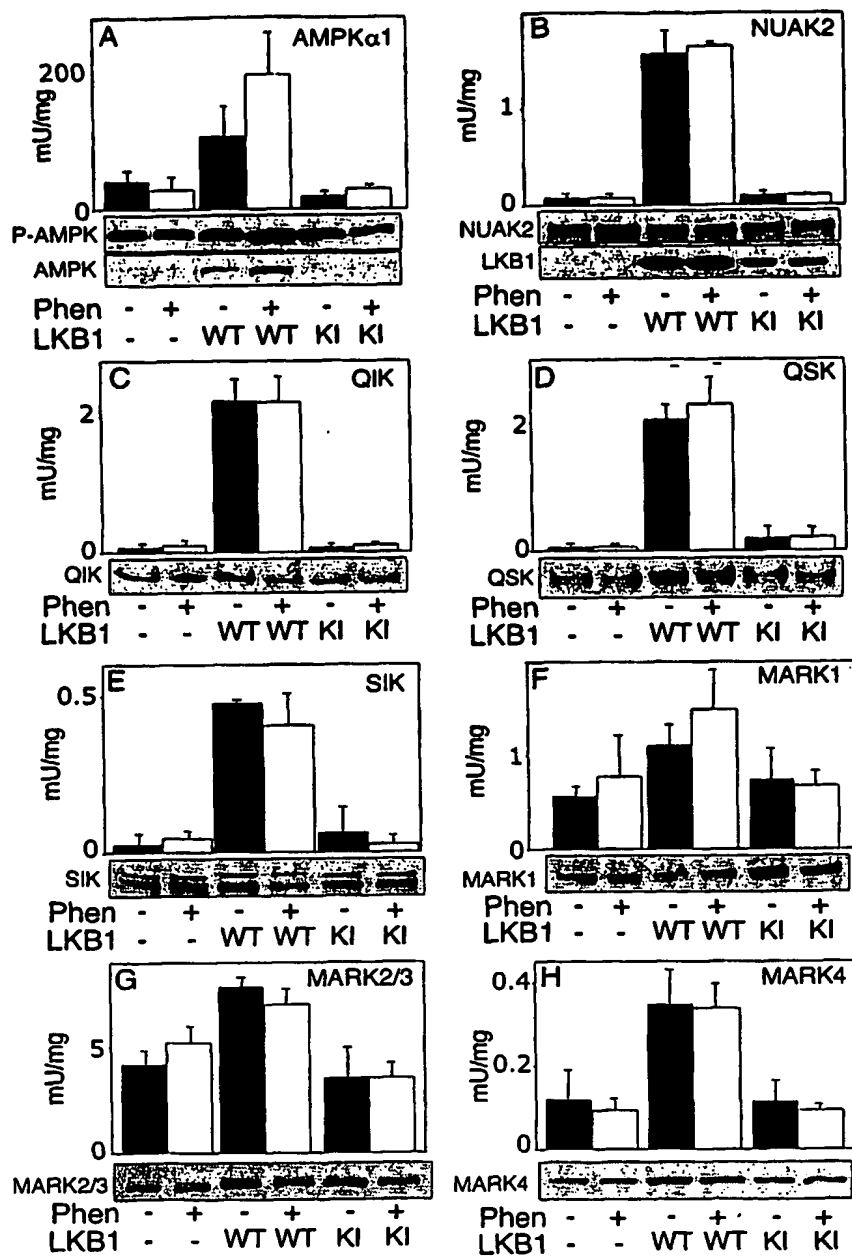
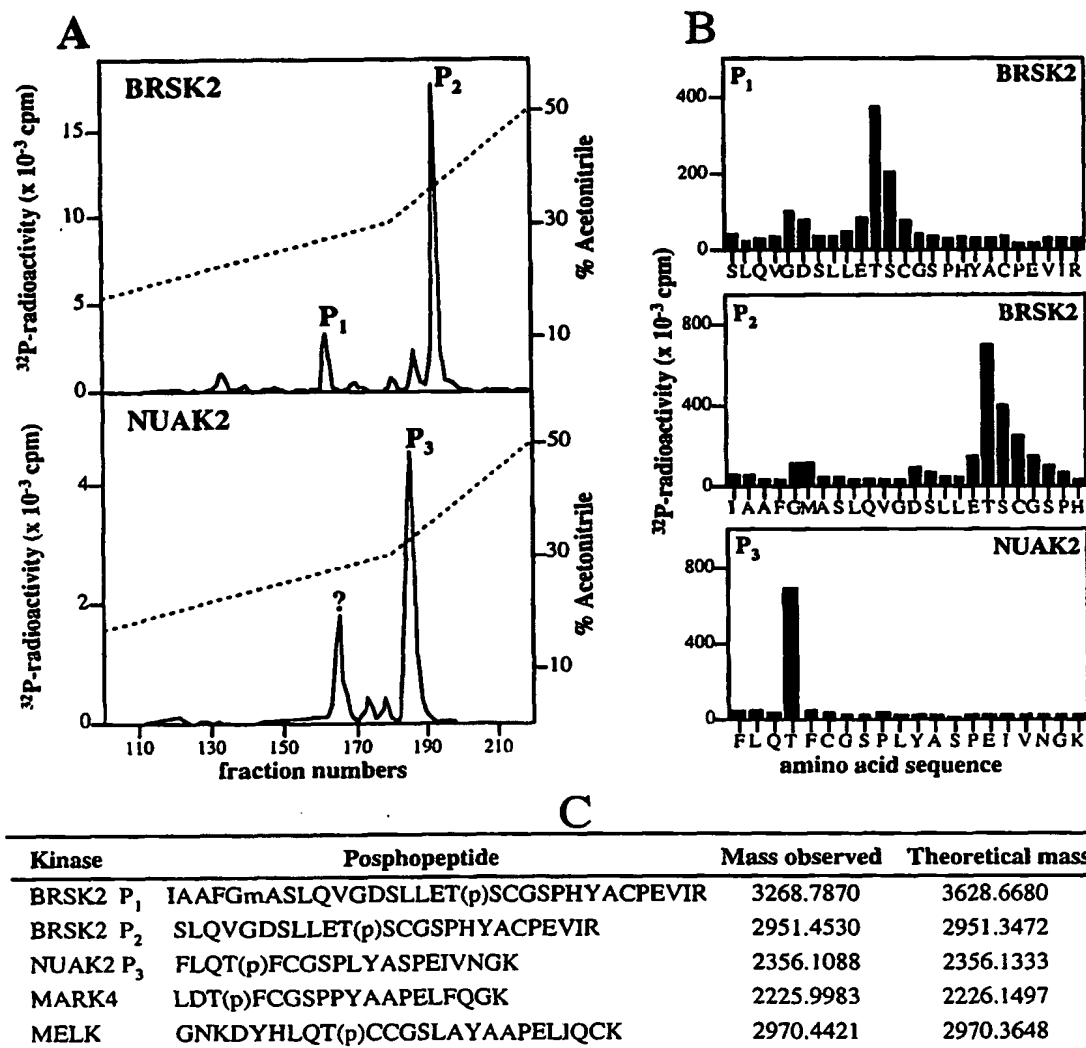


Figure 30



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